biologic effects and health hazards of microwave radiation

PROCEEDINGS OF AN INTERNATIONAL SYMPOSIUM
WARSAW, 15 – 18 OCTOBER 1973

sponsored by
The World Health Organization
The US Department of Health,
Education and Welfare,
The Scientific Council to the Minister
of Health and Social Welfare, Poland

Polish Medical Publishers

The symposium was held to facilitate the exchange and evaluation of current information about the biologic and health effects of microwave radiation, and, in this way, to focus attention on those areas in which additional information is needed and new approaches can be developed. Sixty participants from 12 countries took part and 39 scientific papers were presented during the four-day period October 15—18, 1973.

Biologic Effects and Health Hazards of Microwave Radiation

Proceedings of an International Symposium

Warsaw, 15–18 October, 1973

Sponsored by:
The World Health Organization,
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The Scientific Council to the Minister of Health and
Social Welfare, Poland

Polish Medical Publishers
Warsaw 1974

This Symposium was supported
by the US Department of Health, Education
and Welfare, Food and Drug Administration
Research Agreement No. 05-609-4

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First edition 1974, Printed in Poland

Symposium Secretariat and Editorial Board

Dr. P. CZERSKI
Dr. K. OSTROWSKI
Dr. M. L. SHORE
Dr. Ch. SILVERMAN
Dr. M. J. SUESS
Dr. B. WALDESKOG*

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* replaced by Dr. E. Shalmon from December 1st, 1973

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Preface

The International Symposium on the Biologic Effects and Health Hazards of Microwave Radiation was held during the four-day period October 15—18, 1973, at a conference center in Jadwisin, near Warsaw, under the joint sponsorship of the Governments of Poland and the United States of America and of the World Health Organization.

The Government of the Polish People's Republic, through the Scientific Council to the Minister of Health and Social Welfare, designated the Institute of Biostructure of the Warsaw Medical Academy to be the collaborating institution; the Government of the United States of America was represented by the Department of Health, Education, and Welfare, Food and Drug Administration, Bureau of Radiological Health, and the World Health Organization was involved through its Environmental Health Programme.

Special assistance in the arrangements for the Symposium was given by Dr. B. D. Blood, International Health Attaché, United States Mission to the International Organizations in Geneva.

The Symposium was the culmination of a two-year exploratory and planning effort to bring together, for the first time, scientists and scientific program directors from the nations known to have research interests in the effects on health of exposure to microwave radiation. This was believed to be important for several reasons: the expanding use of microwave power for an increasing variety of industrial, military, medical, commercial and household purposes; the capacity of microwave radiation to produce demonstrable biologic effects; and the unresolved differences in reported biologic effects and in the exposure and safety standards derived from them.

The objectives of the meeting were: to exchange current information about the biologic and health effects of microwave radiation and recommend further needed research and approaches, to encourage international cooperation in relevant research, to promote the evaluation of scientific information needed for setting safe exposure standards, to consider ways of achieving international dosimetric standardization, and to publish and disseminate the Proceedings.

It was thought that the purposes of the Symposium would best be served by a relatively small group of participants given ample opportunity for formal and informal discussion. Regrettably this excluded participation by many experts connected with research programs concerned with the microwave range of the electromagnetic spectrum (defined for the symposium as 300—300.000 MHz).

Sixty participants from the following countries and from WHO attended: Canada, Czechoslovakia, Denmark, the Federal Republic of Germany, France, the German Democratic Republic, Japan, Poland, Sweden, the Union of Soviet Socialist Republics, the United Kingdom and the United States of America.

Three specialists from Argentina, Czechoslovakia and Israel who were invited to attend the Symposium had to cancel their scheduled participation.

Representatives of several international organizations also attended the Symposium. The participants were scientists and program directors from various institutions, universities, agencies and laboratories concerned with the physical, biomedical and behavioral sciences.

English and Russian were the official languages of the Symposium and a simultaneous translation service was provided. The many multilingual participants and members of the staff provided translations from French and other languages.

Thirty-nine scientific papers were presented in six sessions: A. General Effects of Microwave Radiation, B. Influence of Microwave Radiation on the Nervous System and Behavior, C. Effects of Microwave Radiation on the Cellular and Molecular Level, D. Measurements of Microwave Radiation, E. Occupational Exposure and Public Health Aspects of Microwave Radiation, and F. Future Research Needs, Conclusions and Recommendations. Abstracts of the papers, prepared in advance by the authors, were translated in Poland and distributed to the participants in English and Russian versions before the start of the Symposium.

The spirit of the Symposium was one of goodwill, enthusiasm and genuine interest in interchange with scientists of other countries. The setting of the meeting and housing of participants in a suburban conference center greatly contributed to the success of the Symposium. For many participants it was their first opportunity to meet investigators known to them only through the literature. On several occasions, impromptu meetings by groups of participants were arranged in the evening or early morning to discuss topics of interest not on the program. It was notable that plans were initiated during the conference for some collaborative work and exchange of information and instrumentation by participants of different scientific persuasions.

The controversial issues that have characterized the field for the past two to three decades relate to: (1) the mechanisms of interaction of microwave radiation with biologic systems, (2) the levels and circumstances of exposure capable of producing biologic effects, and (3) the nature and significance of biologic effects.

Differences in approaches and findings, principally between countries in western Europe and North America and those in eastern Europe, have led to considerable variance in microwave exposure criteria and standards. For example, the usual recommended maximum power density level for occupational exposure in the United States is 10 milliwatts per square centimeter, based mainly on the risk of cataract formation from heating effects, in contrast to the standard for full-time work exposure in the Soviet Union of 10 microwatts per square centimeter, based on low intensity non-thermal biologic effects. It was not the intention of this conference to consider discrepancies in standards and compliance, however, but rather to open the way for scientists to present and discuss studies and interpretations that have been the underpinnings of different safety standards and to propose ways of advancing knowledge and understanding in this relatively new field. While differences could not be fully explored, and certainly not resolved, progress was made in clarifying concurrences, delineating areas of disagreement, and identifying needed research, communication and program development.

The session chairmen prepared summaries of their respective sessions and the rapporteurs prepared summaries of the discussion. The session summaries provide specific suggestions for further work in each of the subject areas. The final recommendations reflect the sense of the Symposium and give emphasis to international considerations and broad questions of research and development. In areas where improved international collaboration is needed to advance knowledge and understanding, emphasis was given to the general ways in which this may be accomplished, to the value of an international program in the field, to the critical need for standardization of measurement techniques and dosimetry, to the importance of universal nomenclature and definitions of physical units, and to the usefulness of operational definitions of microwave intensities for comparable approaches to biologic questions. With regard to further research, the need for multidisciplinary studies of interactions and risks was stressed, especially with respect to cumulative and delayed effects, low intensity effects and possible threshold values.

All of the papers presented at the Symposium were submitted by the authors in manuscript form in advance of the meeting. Necessary reduction in length of manuscripts was accomplished with the help of the authors whenever possible. Because prompt publication of the Proceedings was considered important, time did not permit review of proofs by the authors. The Proceedings are published in English only, and all the papers written in Russian were translated into English in Poland.

The Symposium secretariat served as the editorial board for the Proceedings.

The contributions of many individuals and organizations to the planning, conduct and successful outcome of the symposium are gratefully acknowledged. In particular, we note with appreciation the outstanding administrative arrangements for the symposium made by Mr T. Olejniczakowski and his staff; the support and help of the Coordinating Commision for Polish-American Scientific Collaboration and the American Embassy in Warsaw; and the assistance of the administrative and editorial staff of the sponsoring agencies.

Opening Session

K. OSTROWSKI, B. H. DIETERICH, J. C. VILLFORTH

WELCOME TO PARTICIPANTS
ADDRESS ON BEHALF OF THE SCIENTIFIC COUNCIL TO THE MINISTER OF HEALTH AND SOCIAL WELFARE, POLISH PEOPLE'S REPUBLIC

K. Ostrowski

Institute of Biostructure, Medical Academy,
Warsaw, Poland

It is my privilege to open the Symposium on Biologic Effects and Health Hazards of Microwave Radiation. This symposium is sponsored by the World Health Organization, the U.S. Department of Health, Education and Welfare, and the Scientific Council to the Minister of Health and Social Welfare of the Polish People's Republic. It is my great pleasure to greet you all on behalf of the last named body. I would like to acknowledge with thanks the financial assistance of the American co-sponsor. Without this generous help it would have been impossible to organize this meeting.

We are in a very fortunate position to have with us the pioneers in the field of research on microwave bioeffects — Dr. Z.V. Gordon from the USSR and Dr. H.P. Schwan from the USA. The organizers of this meeting tried to invite most experienced workers in this field from all over the world, hoping that this meeting will lead to fruitful discussions and allow conclusions to be drawn for further research and perhaps for medical practice.

May I express my most sincere thanks for their help in organizing this meeting to Drs Charlotte Silverman and M.L. Shore from the U.S. Department of Health, Education and Welfare, B. Waldeskog from WHO Headquarters in Geneva and M.J. Suess from the WHO Regional Office for Europe in Copenhagen, as well as to Dr. B. D. Blood, the U.S. International Health Attaché in Geneva, who was not able to attend this meeting.

Special thanks are due to Dr. P. Czerski, one of the leading research workers in the microwave bioeffects field in this country. Most of you know him from scientific contacts, but all of you will remember his activities as the scientific secretary of this Symposium.

As this meeting starts two weeks after the beginning of the new academic year in Poland, may I be allowed to use for the opening of this symposium the time — honored formula, used for centuries at our universities: "ul felix, faustum fortunatumque sit!".

WHO CONCERN AND ACTIVITIES RELATED TO HEALTH IMPLICATIONS OF MICROWAVE RADIATION

B. H. Dieterich

Division of Environmental Health, World Health
Organization, Geneva

It gives me great pleasure to welcome you to this International Symposium on Biologic Effects and Health Hazards of Microwave Radiation which is jointly sponsored by the Scientific Council to the Minister of Health and Social Welfare of the Polish People's Republic, the Department of Health, Education, and Welfare, USA and the World Health Organization. I should like to convey to you the greetings of Dr. Mahler, the Director-General of WHO, and of Dr. Kaprio, the Director of WHO's Regional Office for Europe.

Before coming to the specific subject of this Symposium, I should like to emphasize the importance which WHO is giving to protecting human health from adverse influences resulting from conditions in the environment. Human environment has become lately of concern to governments and people all over the world, and great efforts are being made to understand more clearly, and if possible quantify, the relationship between the environment and man. Large programmes have been initiated in many countries and large amounts of money are being invested in controlling environmental pollution and in protecting and promoting human health by means of environmental control.

As WHO has noted in its Fifth General Programme of Work for the period 1973—77, man has always had to face the problems of his physical environment but — at the beginning of the century — these problems underwent rapid changes. As the progress of science and technology has provided man with the possibilities of more rational approaches and more effective tools to conquer nature, he has attempted to create certain control mechanisms in order to adapt himself to the changing situation. In the contemporary world he has been faced with greater challenges than ever before. Old environmental hazards still prevail in many parts of the world hampering basic health progress in the developing countries in both their rural and urban areas. New problems, however, have emerged that need increasing attention by WHO The air in urban and industrialized areas is being heavily polluted by automobiles, aeroplanes, power generators, heating equipment, and refuse incinerators. The microclimates produced are being further impaired by thermal inversion and photochemical changes induced by solar energy. Rivers are being polluted not only by an increasing variety and amount of inorganic, synthetic, organic and radioactive compounds in industrial wastes, but also by chemicals used in agriculture and by domestic detergents. Oceans have not been spared either and the poisoning of aquatic life together with the export of seafood have created health problems even in the parts of the globe far away from the site of pollution.

Adverse environmental influences include also physical and social stresses associated in some countries with rapidly increasing urbanization and industrialization, such as crowding, slums, noise, behavioral disorders and accidents. Man at work has been faced with occupational hazards in industrial plants, as well as in small-scale rural industries, particularly in those countries which have not yet been able to develop adequate occupational health services suitably equipped and staffed with health personnel. Therefore environmental problems nowadays must be attacked on a much broader front.

Within this framework, this Symposium has been organized to bring together available knowledge on the biological effects and health hazards of microwave radiation. For the last five years WHO has been concerned about the health implications of the growing use of devices producing non-ionizing radiation, and particularly microwave radiation. In view of the potential magnitude and significance of environmental pollution from microwaves there appears to be a need for national and international public health programmes concerned with the evaluation and control of human exposure to microwave radiation — programmes that will reflect the rapid technical development of devices emitting such radiation. There is a pressing need for internationally agreed criteria and standards of exposure on which to base any control programme. Many questions still remain to be answered before such an agreement can be reached. These include more research on the effects of microwave radiation on human health and the development of techniques and instrumentation for the determination of the exposure and dosimetric parameters to achieve quantitative research. The review and evaluation of existing knowledge made by this Symposium will aid WHO in suggesting priorities and reviewing the long-term programme on microwave radiation. Also, it is expected that identification of the researchers and organizations involved in the study of microwave radiation and the promotion of contacts between them during this Symposium will improve the necessary exchange of information on research in this field.

We are, therefore, looking at this Symposium as a step forward in this joint effort undertaken by the scientists in various countries and WHO to bring together scientific achievements in different parts of the world and to establish on this basis recommendations to respective governments which should ultimately lead to the control of potential hazards from radiation.

I hope that this Symposium will make in important contribution in the field of science and will promote further cooperation between the participants and WHO.

I wish you success in the task ahead of you.

U. S. PUBLIC HEALTH SERVICE CONCERN AND ACTIVITIES RELATED TO HEALTH IMPLICATIONS OF MICROWAVE RADIATION

J. C. Villforth

Bureau of Radiological Health, Food and Drug Administration, U.S. Department of Health, Education, and Welfare

The population is being exposed to a rapidly increasing number of devices which emit potentially hazardous radio frequency (RF) and microwave radiation. The availability of these devices in consumer, medical und industrial applications is increasing. The biological effects of low-level microwave exposure are not well documented or understood. The state-of-the-art in manufacturing processes to develop new and improved RF and microwave devices has far exceeded the developmental aspects of radiation detection instruments necessary to measure these frequencies of radiation and the biological research efforts to determine the potential somatic or genetic risks from these devices.

As a result of these and other concerns, the Radiation Control for Health and Safety Act was passed in 1968, and the primary responsibility for administering this Act was delegated to the Bureau of Radiological Health in the U. S. Public Health Service. The Act requires the Bureau to conduct research into the health effects from electronic products radiation (including microwaves) and to establish and enforce standards of performance for electronic products that will assure that the public health and safety are protected.

The concerns for protection from microwave radiation have also been manifest in the functions of two other federal agencies in the USA. The Environmental Protection Agency, established in 1971, is concerned with the effects of the general population exposed to environmental hazards, including microwaves from such sources as radar sites and communication systems. Although the EPA does not have specific authority to establish regulatory standards for these sources, it has general authority to develop guides and recommendations.

The third federal agency is the Occupational Safety and Health Administration of the U. S. Department of Labor. This Administration is charged with the protection of the workers from occupational insults, including microwaves. They have under consideration occupational exposure limits for the working environment. This organization is not, presently, conducting research in the biological effects of radiation.

Although it is the intent of this Symposium to keep within the area of biological effects and health hazards of microwaves, I feel it would be of interest to mention some of the activities of the Bureau of Radiological Health related to microwave radiation.

Within the broad microwave frequency band the most immediate public health problem in the United States was that associated with microwave ovens; therefore, a high priority was given to the assessment of the potential hazard of this microwave emitter which was designed to be used in the domestic and institutional preparation of food. Initially there were no commercially available instruments which could be utilized to quantitate the energy in the specific frequencies used by microwave cooking ovens. Efforts to remedy this deficiency were carried out in our laboratories as well as under contract with other Federal agencies and commercial establishments. Existing engineering as well as biological laboratories of the Bureau had to be remodeled to permit work on this new problem. The Bureau began instrumentation development for microwave research, concentrating on 2450 MHz — the frequency most commonly used in ovens. Instrumentation was essential for both radiation characterization and biological research activities. An anechoic chamber was designed and constructed to provide for near and far field 2450 MHz exposures. Instruments were designed, fabricated and tested to monitor radiation in the chamber. Special field survey instruments were also constructed. Most of the bioeffects work conducted by the Bureau has been restricted to this frequency for which instrumentation is now available.

Simultaneously with developmental work on measurement and dosimetry capabilities, the Bureau commenced a laboratory investigation to assess the performance parameters of microwave cooking ovens and to determine the engineering variabilities which affected radiation emissions. Product evaluation in the laboratory was paralleled by field investigations and manufacturing plant visits.

The Bureau's biological and engineering specialists established the need for a standard, defined the permissible leakage levels associated with it and made the essential determination of feasibility. All existing knowledge was evaluated to provide a sound scientific basis for the microwave standard. This basis was successfully defended against the scientific arguments which were developed primarily by the affected industry. The Bureau published the microwave oven performance standard in the Federal Register on October 6, 1970. The standard became effective in October of 1971. The scientific basis for the microwave oven performance standard has been recognized as a significant achievement in support of the general product safety activities of the United States; however, the emission limit of 1 mW/cm^2 measured at 5 cm from the surface of a new oven is for a single product (cooking oven) which operate at two specific frequencies

(915 and 2415 MHz) and should not be confused with occupational exposure standards used in the USA and other countries.

The Bureau is concentrating on its enforcement activities in support of the microwave oven standard. These activities include continued efforts in the laboratory compliance and endurance testing programs as well as continuous review and evaluation of manufacturers' certification and testing programs. This latter function will consist of both administrative evaluation of submitted reports as well as site inspections of testing and quality control programs at the point of manufacture.

The second part of the program is the complementary biological research in the RF microwave area. The following biological research areas are being pursued:

Epidemiologic studies. Evidence pointing towards a correlation between fathers working at radar installations and the incidence of mongolism in their progeny has been examined.

The study is not complete, but preliminary indications are that the original correlation may not be supported. An epidemiologic study is under consideration to determine if cataracts or other lens opacities are associated with the therapeutic application of microwave diathermy in medical and dental practice.

Pathologic studies. Investigations are under way on both the direct and secondary ocular effects of microwave exposure. Rabbits and a genetically-determined cataractogenic strain of mice are being used as test animals. The mouse strain is being utilized in studies of effects of chronic, low-level exposures.

Research in microwave teratogenesis is under way with positive results at high doses. Research with the fetus has also revealed some marked and persistent effects on the bone marrow. Therefore, hematological observations are also being made. Studies of rodent testes are aimed to provide comparisons between effects of different sources of heat, including microwaves, infrared and conducted heat. Suggestive evidence has also been obtained to indicate persistent testicular effects in mice which received chronic low-level exposure averaging about 6 mW/cm^2.

Metabolic studies. Research is directed toward the biochemistry of the central nervous system, and of fetal development. Microwave induced changes being examined include total protein and myelin content of brain. Some specific molecular species changes, such as changes in absorption spectra of irradiated albumin in both *in vitro* and fetal blood systems, require additional study.

Neurophysiologic studies. Baseline observations of normal behavior in tasks involving learning, memory, alertness and arousal continue, and dose-response curves relating absorbed microwave power and performance will be compiled. Data obtained up to now suggest that some of the microwave effects have their origins in neurochemical processes. Techniques to measure neurochemical transmitters are being developed.

Genetic studies. More informative procedures for survival assays have been identified so that the killing efficiency of microwave irradiation of cells in culture can be determined. Techniques have been developed to examine lethality from the absorption of energy by water in comparison with possible effects that may have been masked by absorption. In addition studies have been initiated to measure the effects of microwave irradiation on genetically determined temperature-sensitive enzyme systems. These enzymes may be useful in further studies of effects of protracted exposures.

Dosimetric studies. Laboratory experience with animal irradiation has led to the development of a controlled environment semi-automated waveguide irradiation apparatus for which integral dose rates and absorbed doses can be determined for each exposed biological specimen. Currently being developed is a laboratory for determining the distribution of absorbed dose in biological specimens and in anatomically realistic phantoms of animals.

The technical problems encountered by the Bureau in its investigations of microwave ovens, specifically the lack of nearfield measurement devices for 915 and 2450 MHz, is indicative of the general hardware problem associated with all non-ionizing radiation investigations. The manufacturing industry utilization of recent technical developments to produce electronic products for consumer, medical, industrial, and educational applications, has not been matched at all times by a concern for radiation safety. The net result of this situation is that the Bureau, in many cases, is forced into a research and development activity in order to produce the necessary product evaluation information from which dosimetry systems can be developed in order to assess the present or potential deleterious biological effects from exposures to these radiations.

Although the Bureau has promulgated a performance standard for microwave ovens, a great deal of research is required to assess the differences of opinion related to low-level exposures to microwaves. We have only scratched the surface in developing a biological effects program with respect to microwaves, and it should be noted that even this minimal effort is only being directed at the frequency (2450 MHz) which is utilized for microwave cooking ovens and for which instrumentation is available.

Session A. General Effects of Microwave Radiation

Chairman: *H. P. Schwan*
Vice-Chairman: *Z. V. Gordon*
Rapporteurs: *T. V. Kalada and M. L. Shore*

THERMAL EFFECTS OF SINGLE AND REPEATED EXPOSURES TO MICROWAVES — A REVIEW*

S. M. Michaelson

University of Rochester, School of Medicine and Dentistry, Department of Radiation Biology and Biophysics, Rochester, New York, U.S.A.

INTRODUCTION

Review of the literature on biologic effects of microwaves reveals several areas of established effects and mechanisms on the one hand and speculative effects and mechanisms on the other. This has created a dilemma in trying to assess the real or imaginary from the actual or potential hazard to man from exposure to this energy. Part of this dilemma is based on semantic differences and/or lack of appreciation of past scientific achievements as well as a lack of conceptual approaches in the planning and/or analysis of studies.

Although most of the experimental data support the concept that the effects of microwave exposure are primarily a response to altered thermal gradients or hyperthermia, there are large areas of confusion, uncertainty and actual misinformation. To put the question of microwave bioeffects in its proper perspective, a critical analysis of the published literature is essential to differentiate the known and substantiated from the speculative and unsubstantiated effects.

BIOPHYSICS

For this presentation, microwaves will be defined as that portion of the electromagnetic energy spectrum encompassing the frequency range of 300 MHz — 300 GHz with

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* The work upon which this paper is based was performed pursuant to Contract No. FDA 73-30 with the Public Health Service, Food and Drug Administration, Department of Health, Education and Welfare, with support by the Bureau of Medicine and Surgery, U.S. Navy, and with the U.S. Atomic Energy Commission at the University of Rochester Atomic Energy Project and has been assigned Report No. UR-3490-317.

wavelengths in free space of 1 meter to 1 millimeter. In order to understand the consequences of microwave exposure, consideration of biophysical principles and mechanisms of action is essential. These will be presented by Drs. Schwan and Illinger.

THE PHYSIOLOGY OF THERMAL REGULATION

The mammal is a complicated self-regulating organism, composed of different organs with diverse cell types. The effects of heating can be subdivided into those acting at (a) the cellular level, (b) the organ level, and (c) the total self-regulatory mechanism. When we are dealing with the whole organism, the effects at all these three levels occur simultaneously and are more or less interrelated (10).

One of the main factors in temperature regulation of mammals is their capacity to alter the temperature gradient between the "shell" (peripheral) and the core (deep tissue) of the body. That a gradient exists at all is due to the fact that the body loses heat from its surface by conduction, convection, radiation and evaporation (9).

It is appropriate at this time to define what I mean by thermal effects, namely effects that result from heating of tissue through the application of electromagnetic fields. The effect may be a result of, or a response to, heating the body, a specific organ, or a controller (i.e. nerve, blood vessel, endocrine organ) of an organ or body system. This definition also invokes the concept that selective heating or alteration in thermal gradients may occur which may not necessarily manifest themselves by a measurable increase in core or colonic temperature. The basis for this definition is that thermal gradients in the body can vary under normal circumstances. The body, however, has the physiologic capability to accommodate to such changes without a change in core temperature. The core temperature of a mammal can remain constant when the heat generated by the metabolism of the body is equal to the heat lost from its surface (16). As both the rates of heat production and of heat loss vary in different tissues and organs of the body, local temperatures also vary. Generally, temperatures of peripheral tissues are lower than those of deep tissues, but both peripheral temperature and core temperature reflect unmeasurable means of many different temperatures (3).

Gordon and Tolgskaja (14, 38) define thermal as the presence of an overall heat effect as measured by the core temperature response of the animal. Such temperature implies an integral thermal effect reflecting thermoregulation in the entire body. It is important to realize, however, that the absence of a temperature rise in the colon does not exclude the possibility of such an effect in tissues and internal organs absorbing microwave energy. Although the rectal temperature is a reasonably representative measure of deep body temperature in steady state conditions, it is slow to indicate changes in body temperature, and its use cannot be recommended for thermoregulatory studies of the relations between thermal stimuli and thermoregulatory responses (3).

The temperature control system is an example of a dynamic system approaching the accuracy of an engineered one (12). All the complicated mechanisms of heat regulation are integrated by hormonal and nervous control as well as by a direct temperature effect of the blood supplying the hypothalamus which can also be influenced experimentally by direct heating. The threshold for direct heat activation is an increase in temperature of 5 to 6°C (10).

Temperature changes can act as stimuli to different organs, influencing their behavior. The rate at which the heat is dissipated will vary in different species depending on heat-regulating mechanisms or metabolic characteristics. The breakdown of protective mechanisms for heat control causes an uncontrolled rise in body temperature.

The maintenance of a certain temperature is of vital importance to the organism because all biologic processes are conditioned by temperature. The temperature of the tissues is an important factor which determines the extent of the physiologic response to heat. Below a certain temperature threshold, no reactions are observed. A change in tissue temperature could produce a change in the degree of the physiologic response.

Specific organ or tissue systems may "function" at a significantly different rate if local thermal gradients are altered. Based on an extensive review of the literature on thermal regulation, Thauer (37) concluded that relatively large changes in circulation are provoked by quite small deviations from neutral temperature. Also, the cardiovascular system is subject to the combined influence of both skin temperature and deep temperature. Under certain conditions, the thermal stimuli to the skin can be of greater significance in causing cardiovascular reactions than the level of core temperature.

Within a few degrees, nerve fiber transmission rates are temperature dependent (6, 42). In mammals the central nervous system ceases to function at 44 to 45°C and the heart stops beating at 48°C. A rise in temperature of 5°C causes a twofold to threefold increase in pulse rate, oxygen consumption, etc. The mechanisms of heat regulation are activated in several ways: by thermal receptors in the skin, by direct stimulation of the hypothalamus, and by receptors in the spinal cord and viscera.

Heat receptors are distributed in a definite pattern in the skin. Sensory summation may occur so that the threshold for stimulation decreases as the size of the area stimulated increases. Sensations occur for changes in temperature of a few thousandths of a degree in a second (12).

THERMAL EFFECTS OF MICROWAVE ABSORPTION

In assessing the biologic effects of microwaves, it is essential that the investigation be well-conceived and appropriately conducted, and that an intelligent relationship of exposure to an appropriate biologic endpoint be established. It is difficult, however, to extrapolate to larger animals or man from small laboratory animals with differences in methods and capacities of thermal regulation, different absorption cross section, body size, surface area, and with differences in energy distribution within the body and in metabolic rates.

Under normal circumstances, animals have an average rate of physiologic cooling, whether they are active or at rest, which is determined by (a) geometry — ratio of body volume to surface area, (b) insulating factors — fur or hair, and (c) environmental factors — i.e. temperature differences between the body and its surroundings. The absorption of microwave energy in the animal manifests itself in the form of heat. The irradiated animal must compensate for this heat input or else suffer a rise in body temperature.

The extensive investigations into microwave bioeffects during the last 25 years conclusively show that exposure to power density of 100 mW/cm^2 for several minutes or hours, depending on the animal species, can result in pathophysiologic manifestations of a thermal nature characterized by a temperature rise which is a function of the thermal regulatory processes and active compensation of the animal. The end result is either reversible or irreversible change depending on the conditions of the irradiation and the physiologic state of the animal. At power densities below 100 mW/cm^2, however, evidence of pathologic change is nonexistent or equivocal for large animals (24, 25).

Temperature increase in the body during exposure to microwaves depends upon the following factors: (a) animal species, (b) the specific area of the body exposed and the efficiency of heat elimination at that site, (c) thickness of skin and subcutaneous tissue,

(d) body type or mass and covering of exposed areas, (e) orientation or position in the electromagnetic field, (f) intensity or field strength, (g) duration of exposure, (h) frequency or wavelength of the energy, (i) environmental temperature, air currents, humidity, (j) condition of the exposed subject, such as state of health, method of restraint, anesthetization or other medication (32, 33).

In partial-body exposure, under normal conditions, the unexposed portion acts as a cooling reservoir to stabilize the temperature of the exposed part. This stabilization is due to an equilibrium established between the energy absorbed by the exposed part of the body and the amount of heat carried away from that area. The heat is transported via increased blood flow to cooler parts of the body that are maintained at normal temperature by heat regulating mechanisms. If the amount of absorbed energy is in excess of the optimal amount of heat energy which can be handled by the mechanisms of temperature regulation, a continuous temperature rise, and under some circumstances local tissue destruction, can result (32, 33).

The thermal response of male Long-Evans rats (350—425 g) exposed to 2450 MHz (CW) in an anechoic chamber maintained at 22°C is shown in Figure 1. All rats were pre-handled and gentled for two weeks prior to exposure. The body temperature was allowed to equilibrate in the chamber for three hours before irradiation. After 15 minutes in the chamber, the colonic temperature showed an increase which required three hours to return to baseline (17). The results of exposing rats to 9 mW/cm^2, 18 mW/cm^2, and 36 mW/cm^2 for 150 minutes are shown. The 9 mW/cm^2 level caused a distinct colonic temperature rise, when compared to the sham-irradiated group. A similar temperature response in rats exposed to 2450 mHz (CW), 10 mW/cm^2 has been reported by Djordjevič and Kolak (8). Incident energy of 18 mW/cm^2 caused approximately twice the temperature rise as 9 mW/cm^2. All of the temperatures demonstrated in the irradiated rats were within a range observed in the first fifteen minutes of the equilibration period. Exposure to 36 mW/cm^2 caused a fourfold increase in colonic temperature. These data suggest the lability of the temperature response of rats as a result of experimental manipulation and the importance of ascertaining the relation of the expo-

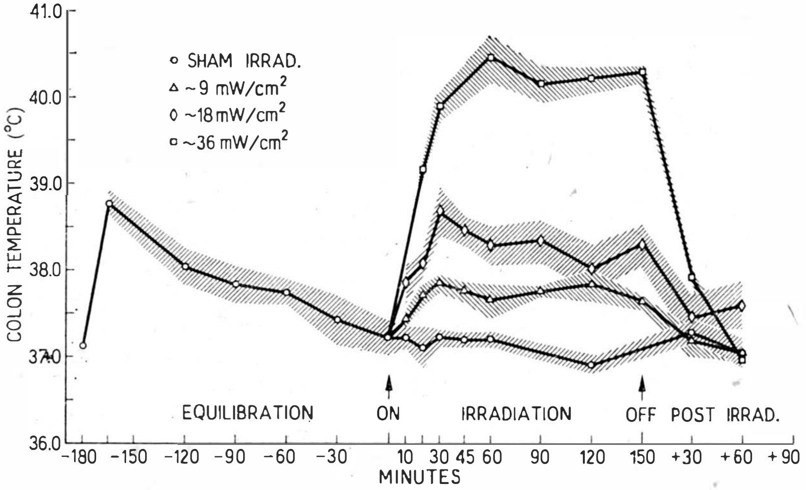

Fig. 1. Colonic temperature response in rats exposed to 2450 MHz CW microwaves.

sure to the equilibration period in studies involving temperature measurements in rats exposed to microwaves.

The thermal response in the dog exposed to 165 mW/cm², 280 MHz pulsed (360 pulses/sec, 2—3 μsec pulse width) at 30% humidity consists of three phases (25) (Fig. 2). In phase 1, initial thermal response, body temperature increases by 1—2°C, ½ hour after onset of exposure. In phase II, period of thermal equilibrium, rectal temperature stabilizes; this may last 1 hour, during which the temperature will cycle between 40.6 and 41.1°C. In phase III, period of thermal breakdown, the temperature rises above 41.1°C, continues increasing rapidly until a critical temperature of 41.7°C, or greater, is reached. If exposure is not stopped, death will occur. Exposure of dogs at 100 mW/cm² for periods up to 6 hours does not cause a critical rectal temperature. Initial heating is slight, the animal remaining in thermal equilibrium during the remainder of exposure (Fig. 3).

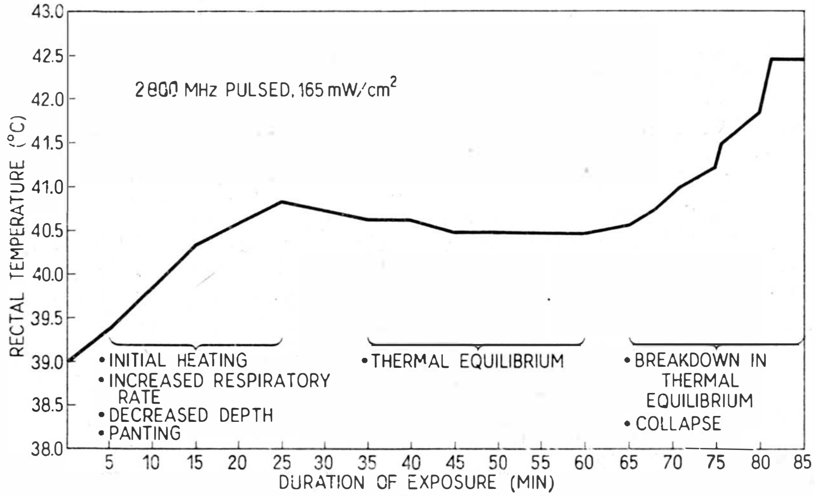

Fig. 2. Thermal response of the dog exposed to 2800 MHz pulsed microwaves, 165 mW/cm².

On the basis of observations on rats exposed to microwaves, Gordon (13) has concluded: (a) there is an inverse relationship between the microwave intensity and the elapsed time until death of the exposed animals; (b) the reaction of animals to micro-

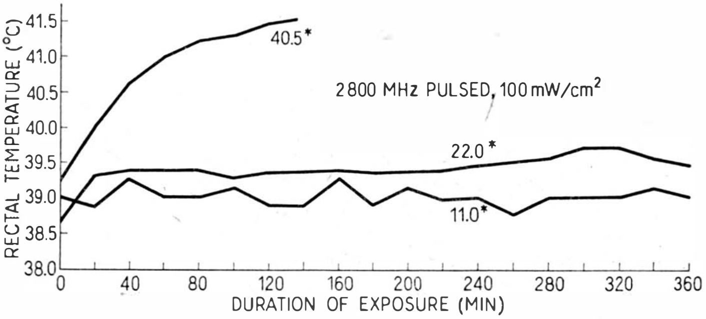

Fig. 3. Response of dogs exposed to 2800 MHz pulsed microwaves, 100 mW/cm² at various environmental temperatures*.

wave exposure always involves the following three periods: an orientation period, an excitation period, and a passive period (with occasional spasms) leading to death from hyperthermia; (c) hyperthermia is due to absorption of the incident energy and its conversion to thermal energy by dielectric losses in the tissues; there is evidently also a direct effect of microwaves on the thermoregulatory centers; (d) the most rapid lethal outcome is produced by irradiation with 10-cm waves of high power density; the effect of decimeter, 3-cm and 5-mm waves is less pronounced; (e) for the same power density of 10-cm waves, lethality is higher and more rapid with pulsed than CW waves; (f) the survival of animals exposed to microwaves, of even low power density, may be affected by changes in their diet or water intake. Irradiation impairs the animal's tolerance to subsequent physical stress. Temperature response obtained by Gordon (13) is shown in Table 1. She showed that for a constant exposure time of 15—30 min, decimeter (dm), centimeter (cm) and millimeter (mm) waves produced rises in rectal temperature at different threshold intensities. The limiting suboptimal power densities were respectively, 5—7 mW/cm^2 for mm waves, 10 mW/cm^2 for 10-cm waves and $>$40 mW/cm^2 for dm waves. A comparable wavelength dependence of thermogenesis has been seen in the dog where 2800 MHz pulsed caused a greater thermal effect than 200 MHz CW (Fig. 4).

Table 1

Increment of Body Temperature upon Exposure of Rats to Continuous or Pulsed 10-cm Waves for 30 Min*

Irradiation intensity (mW/cm^2)	CW $\lambda = 10$ cm	Pulsed $\lambda = 10$ cm
	Δt (°C)	Δ (°C)
2.5	−0.3	−0.2
5.0	−0.2	−0.3
7.5	−0.3	−0.1
10.0	+0.3	+0.1
control animals	−0.1	−0.1

* From Gordon (13).

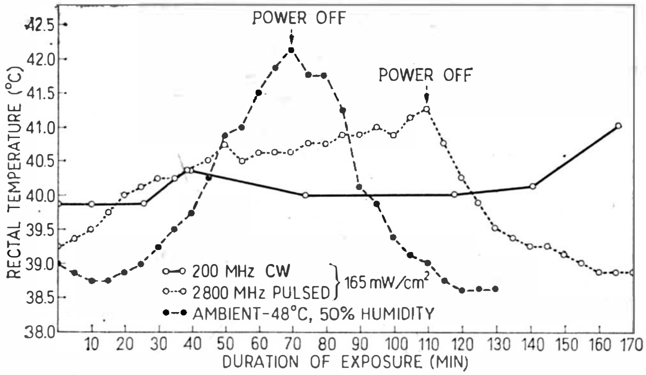

Fig. 4. Comparison of the thermal response of the dog exposed to 2800 MHz pulsed and 200 MHz CW microwaves, 165 mW/cm^2.

The influence of body size

Evidence is available on the relationship of species or body size and sensitivity to microwaves. The survival time of rats exposed to microwaves (13) is noted in Table 2. In contrast, exposure of dogs to 2800 MHz pulsed, 100 mW/cm² could be continued for 6 hours or more (Fig. 3). The apparent greater sensitivity of smaller animal species (rats and rabbits) can be seen in Figure 5. Although a greater sensitivity of rabbits and rats is shown, it is not quite clear whether it is only the body size which is a factor or whether specific differences in physiologic regulation among species may play an equally important part in the response (25). In whole-body exposure of different species of animals, Tjagin (39) demonstrated that the response was dependent not only upon the power density but also upon the animal's size and the quality of its thermoregulatory apparatus. Exposure to 300 mW/cm² raised the rectal temperature by 1—1.5°C in dogs, 6.6—7°C in cats and rabbits, and 7.9—10°C in rats. Subbota (36) noted that of the variations in respiration, pulse rate and blood pressure of dogs exposed in short-term ex-

Table 2

Survival Time of Rats Exposed to Microwaves*

Wave range	Time of death (min)		
	100 mW/cm²	40 mW/cm²	10 mW/cm²
Decimeter	60 (50%)	Survived for 2 h	Survived for 5 h
10-cm	60 (100%)	40 (50%)	Same
3-cm	110 (50%)	Survived for 3 h	,,
Millimeter	180 (50%)	Same	,,

* From Gordon (13).

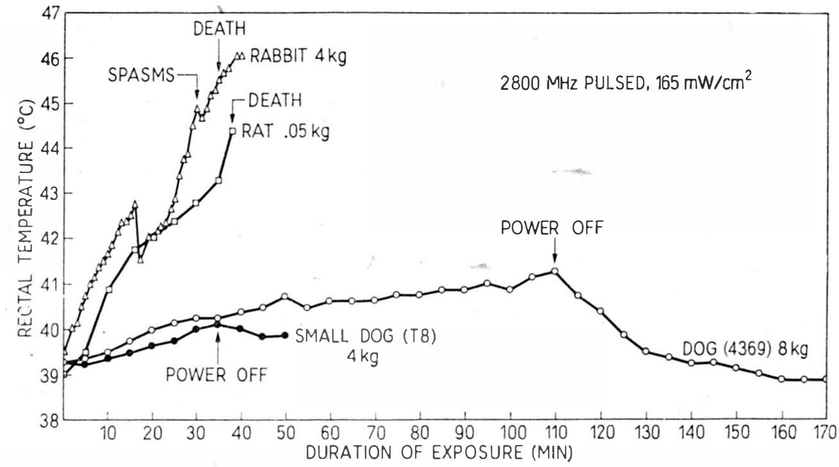

Fig. 5. Thermal response of various species of animals exposed to 2800 MHz pulsed microwaves, 165 mW/cm².

periments to high power densities (200—300 mW/cm²), the blood pressure was the most stable parameter. Other experimental animals (cats and rabbits) were killed by such intensities. At 10 mW/cm² no changes in the cardiovascular system appeared. These results emphasize the need for appropriate scaling, gauging or proportionality factors that have to be invoked in any interspecies comparison of microwave bioeffects among laboratory animals and especially between animals and man.

Thermal gradients and distribution of heat

The distribution of heat induced by microwaves in the body and particularly the brain has been of interest to various investigators using models and confirming the results by animal experimentation (15, 18, 19, 34). These investigations and their implications will be discussed by Drs. Schwan and Guy.

Using the percentage of EM energy absorbed in various body tissues which can be estimated approximately from the electric parameters of the tissues, Presman (30) made calculations for the case of exposure of the occipital region of the head of man, rabbits, and rats to EMF's of superhigh frequency. He found that the amount of energy that penetrates into the subcortical structures varied according to animal size (Tab. 3).

Table 3

Percent of Microwave Energy that Penetrates into Subcortical Structures of Various Animals*

	1000 MHz	2000 MHz	4000 MHz
Rat	30	20	5
Rabbit	20	10	<5
Man	5	<5	0

* Estimated from Presman (30).

In considering the implications of these studies it is important to realize that brain temperature is not uniform. There is a gradient of approximately $^1/_2$°C between surface and deep brain structures (7). Further, the brain regions which are directly sensitive to temperature (i.e. central thermodetectors) and control peripheral thermoregulatory mechanisms during heat stress are located in the anterior hypothalamus/preoptic area (AH/PO) (21). Since microwave power absorption in the brain is non-uniform owing to the nature of EM/tissue interactions and the possibility of hot spots, the choice of brain location for temperature measurement will materially affect the results. It should also be pointed out that so-called core or high colonic temperature is a poor substitute for brain temperature. Numerous reports, where cranial and rectal temperatures were simultaneously measured, have demonstrated that the temperatures diverge with unpredictable phase and amplitude differences (1).

Brain temperature elevations more than about 2°C above set-point are sufficient for paradoxical thermoregulatory responses (20). Successful thermoregulation takes place within this span of AH/PO temperature increases. Once beyond this range, the hyperpyrexia could become irreversible due to positive feedback. It has been demonstrated that 0.1°C is the smallest temperature elevation with physiological significance. Von Euler (40) has shown that a 0.1°C elevation in anterior hypothalamus/preoptic area temperature results in the generation of a 100 mV steady potential in that structure.

Peripheral evidence of heat loss mode processing by central thermoregulators occurs with about $^1/_2$ to 1°C AH/PO temperature elevation (35).

In essence, investigations of the distribution of heat reveal that analysis of microwave bioeffects and attempts to extrapolate them to man must take into consideration the importance of animal size, thermal gradients and species differences in regard to brain circulation and regulation of brain temperature. It is apparent that physiologic responses to subtle temperature changes may occur in small animals which have no relevance for larger animals and man.

Repeated exposures — compensation, adaptation or acclimatization

Gordon (13) has reported that rats exposed to sublethal levels (10 mW/cm²) of mm, cm or dm waves showed greater tolerance to repetitive exposures and were in a satisfactory state after 5—10 sessions. She suggests that presumably the increased tolerance is due to compensatory mechanisms that are called into play.

A similar pattern has been observed in dogs exposed to 2800 MHz or 1280 MHz pulsed. Repeated exposures to 165 mW/cm², 2800 MHz pulsed resulted in improved tolerance as evidenced by the ability to successively prolong exposure time with minimal increase in temperature and progressive depression of "basal" temperature (Fig. 6). Exposure of dogs to 1280 MHz pulsed, 100 mW/cm², six hours/day, five days/week for four weeks revealed an increase in rectal temperature during each exposure for the first week. During the subsequent three weeks, temperature increases were moderate. A progressive lowering of pre-exposure temperature was evident as the number of exposures was increased. Exposure to 50 mW/cm² initially resulted in slight temperature increase. Progressive lowering of the pre-exposure temperatures was noted as the exposures were repeated (Fig. 7).

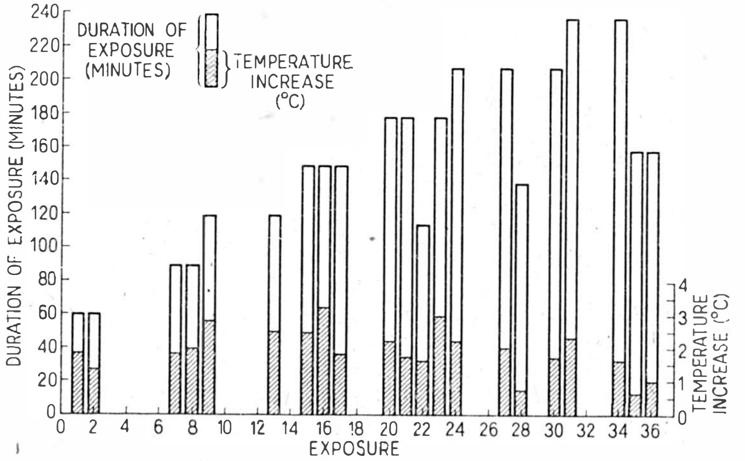

Fig. 6. Microwave tolerance in dogs repetitively exposed to 2800 MHz pulsed microwaves, 165 mW/cm².

Phillips et al. (28) noted acclimatization in rats exposed repetitively to 2450 MHz pulsed (20 mW/cm² or 30 mW/cm² estimated) using temperature response, ECG and heart rate as criteria.

In rats exposed to 2450 MHz (CW), 10 mW/cm², 2 hours a day for 30 days, a slight thermal effect and increase in some blood elements occurred during the first phases

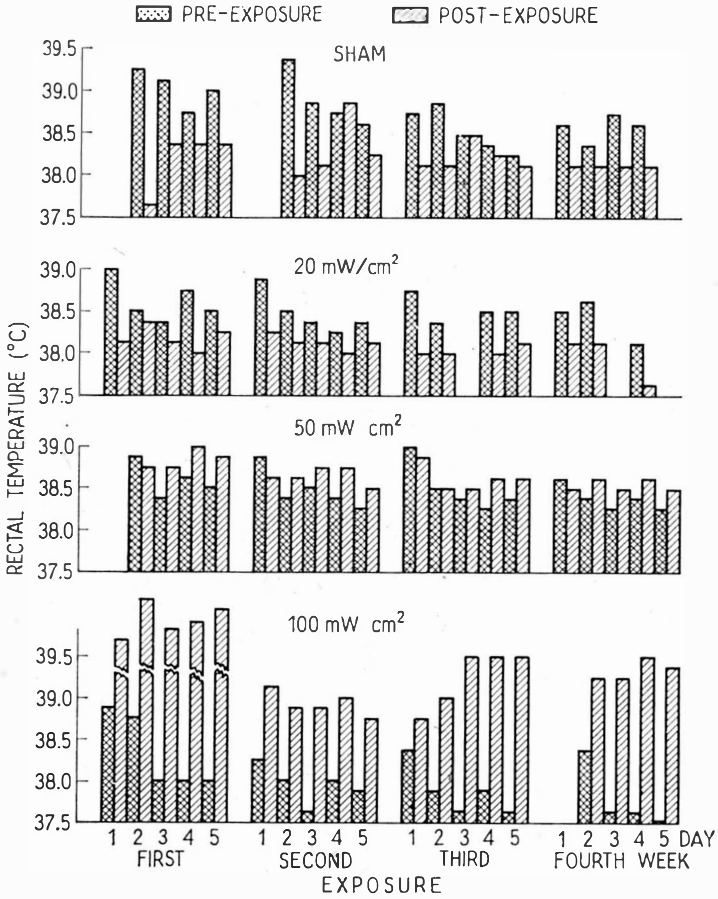

Fig. 7. Microwave tolerance in dogs repetitively exposed to 1285 MHz pulsed microwaves.

of irradiation with a later tendency towards normalization or adaptation (8). Exposure of rats to 3000 MHz at 16—94 mW/cm^2 for 1 min per day led at first to enhanced excitability (after 14—20 exposures) and then to reduced excitability (26, 27).

No cumulative effect of microwaves has been demonstrated if maintenance of adequate thermal regulation is used as the criterion. Intermittent exposure of the normal animal can be tolerated for extended periods of time and is related to the interval between exposures which permits the animal time to recover. These findings of physiologic adjustment to repeated exposures make one ponder the validity or meaning of the reports which suggest cumulative effects of microwave exposure below injury threshold levels.

Cataractogenesis

Thermally induced opacification of the lens of the eye can occur as a result of microwave energy absorption. Dr. Carpenter will review these findings.

I might just point out that careful analysis of the work of Carpenter et al. (4, 5), as well as Williams et al. (41) and Birenbaum et al. (2), reveals that whenever cataracts are produced among animals subjected to different power-density-time relationships, a threshold becomes obvious. No one has yet been able to produce cataracts even by repetitive exposures when the power-density-time relationship is really below threshold.

It is important to note that lens opacity has consistently been produced in only one species, namely the rabbit. Although the rabbit has been traditionally used for studies of microwave cataractogenesis, one might ask whether this species is the most appropriate model? We cannot exclude the possibility that there may be a true difference in threshold values for lens changes in various species *in vivo,* even though this may not be readily or easily confirmed (11). No doubt one also has to be concerned with thermal gradients in the eye. For example, in the normal rabbit, with a corneal temperature of 32.3°C, the aqueous humor will have a temperature of 33°C; the anterior surface of the lens, 33.6°C; the interior of the lens, 35.4°C; the vitreous humor, 36.5°C and the retina, 37°C (31). Such temperature differences have to be taken into consideration when trying to relate cataractogenesis with temperature measurements in the eye. In addition, the metabolism of the eye is influenced by temperature. Thus, interspecies relationship of biochemical constituents has to be taken into consideration.

Neural effects

Reported neural effects and behavioral changes resulting from exposure to microwaves are not necessarily inconsistent with thermogenesis. It should be noted that behavior is not a simple process but is the expression of different effects in various body systems. Temperature input signals arise in many body structures that have been shown to evoke behavioral and/or physiological responses to changes in local temperature.

Pinneo et al. (29) have postulated that many so-called "non-thermal" effects of microwave exposure may actually be specific thermal effects on certain neural structures. They examined the thermal stimulation of peripheral nerves exposed to 3000 MHz and 10,000 MHz microwaves and infrared energies. They showed that all three sources of energy produced the same effects on the central nervous system, and suggested that experiments purporting to show non-thermal effects should be examined with the possibility in mind that a thermally-induced neuro-physiological response may have occurred.

McAfee (23) points out how data can be misinterpreted as the result of some unknown effect of microwave radiation, when hyperthermal effects are not involved. In cats, when peripheral nerves are stimulated by 45°C temperature, adrenal medullary secretion occurs and a rise in blood pressure is developed as a result of adrenal secretion (22). It appears that functional cardiac changes can occur as a result of microwave exposure, no doubt as a response of the autonomic nervous system to the thermal effects. Thermal stimulation of peripheral nerves can produce the neurophysiological and behavioral changes that have been reported. The interaction between the peripheral nervous system and the central nervous system would account for the reported effects on heart rhythm, blood chemistry, etc.

EXTRAPOLATION FROM ANIMAL TO MAN

It is apparent that extrapolation from animal to man is most complex. Observations in the living animal indicate some of the variables that are a result of the interplay of physical factors and physiological controls in a living dynamic system with multiple integrative functions, feedback mechanisms, and redundancy for which the individual relies upon homeokinesis.

One of the problems in studying biologic effects of microwaves, as in all biomedical investigations, is the selection of the most appropriate animal species for study. Animals are quite often selected only on the basis of convenience, economy or familiarity and without regard to their suitability for the problem under study. Because of the lack of awareness and concern in the selection of the experimental animal, many investigations have no inherent value in so far as extrapolation to man is concerned and, in some cases, have led to incorrect interpretations necessitating expensive, time-consuming attempts at confirmation or logical application of the data.

Many animal studies on the response to RF or microwave exposure have been done with small rodents, the responses of which are not readily applicable to human beings, owing to differences in coefficients of heat absorption, different thermal distribution, small body surfaces, and relatively poor thermal regulation in contrast to man who has one of the best thermal regulatory mechanisms.

A comparative approach with appropriate "scaling" or use of proportionality factors is basic to the elucidation of the nature of vital processes among animals and to place man in his proper biological perspective; it relates the different ways in which various species maintain homeostasis, characterizes animals particularly suitable for demonstrating specific responses, integrates and coordinates anatomic, physiologic, biochemical, and pathologic similarities of various groups of animals. From a comparative approach we can learn what biologic attributes are unique or common among different animals, study interrelations with environmental stresses and find animals that are most suitable for study of important functions to provide a basis for biological generalization. It behoves the investigator to become aware of the attributes of various animals to obtain the most meaningful results for studying the effects of RF or microwave exposure so that reliable and relevant extrapolation to man can be made.

CONCLUSION

I would like to conclude on a personal note. We, as scientists, concerned with the biologic effects and health implications of microwave exposure should relate to the concerns and needs of society. It is paramount, nevertheless, that we do not succumb to social and political pressures or aspirations. Science is knowledge based on various activities and disciplines which involve systematic and unbiased observation.

In this year, the quincentennial of the great Polish scientist Nicholas Kopernik (Copernicus), let us not lose sight of the contributions by which he, through penetrating analysis, observations, and mathematical calculations, fought and overcame the prevailing view held since the time of Ptolemy, of the geocentric construction of the Universe and replaced it with his scientifically proved heliocentric theory. Kopernik was followed by other great philosophers of science, such as Francis Bacon in the 16th century, who insisted on the close and methodical observation of facts, setting the basis for a considerable portion of the scientific method. In the 17th century, René Descartes strove to create a new methodology in science based more on deduction than experience, resulting in a monumental discourse on methods. Finally, in the present century, with the thoughts and works of Albert Einstein and his concepts, a system that is mathematically verifiable, based upon time-space relations, is now possible.

From these great philosophers of science the scientific or hypotheticodeductive method has evolved to which we all should subscribe. This philosophy can be separated into four parts which may be classified as: 1) collecting a series of observations, 2) forming an hypothesis that links the observations, 3) testing the truth or falsehood of the hypothesis and 4) using the hypothesis in examination of further observations or re-examinations of those already considered. When the hypothesis answers suitably to repeated or sufficiently delicate tests, we have a finding.

It is disturbing to read certain "scientific" articles or reports which are contrived to convince the reader of the truth of certain views or to put him in possession of certain knowledge. Such works quite often obscure the process by which the expounded views were reached, which usually consists of a series of improvised judgements of working hypotheses interspersed with a provisional series of observations. Many such judgements are normally found untenable and many observations irrelevant, ill-chosen, badly-made or in need of further tests.

In this presentation, an attempt has been made to review, synthesize, and critically analyze the thermal response to microwave exposure. Although there is considerable agreement among scientists, there are lacunae of disagreement. It is highly recommended that apparent discrepancies be studied and analyzed in detail, taking into consideration all the biophysical, biochemical and physiological factors inside the body and external factors that might influence the response of the organism. One must consider the homeokinetic systems that might be involved in regulation as a result of exposure to microwave energy. Free international exchange of information and closer personal contact between scientists would be invaluable in helping to resolve the discrepancies and divergence of opinion that exists in the understanding of some of the biologic and clinical effects of exposure to microwave energy.

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RAPID WARMING FROM HYPOTHERMIA BY MICROWAVES

H. D. Baillie

Crumpsall Hospital, Manchester, England

INTRODUCTION

There has been a plea for further research on the possible nonthermal effects of microwave radiation (1). The importance of this subject in assessing health hazards and establishing safety standards was stressed when strong evidence was presented indicating that nonthermal effects could be cumulative (2).

A recent report suggested that hypothermia could be used for unmasking nonthermal effects during powerful exposures of short duration (3). This suggestion could be applied with advantage.

The following study describes a microwave method for producing rapid warming from hypothermia in the rat. It was developed for investigating the physiological responses to rapid warming but it may prove of value for research on the nonthermal effects of microwaves.

In a preliminary report (4) unmodified exposure of a hypothermic rat in a microwave cavity was shown to produce burns of the animal's extremities. This overheating was prevented by converting the animal's body to a uniform geometric shape by immersing it in a water jacket during exposure.

The final design of the water jacket and details of the rapid warming method are described in this communication.

APPARATUS, METHODS AND MATERIALS

Wistar rats weighing between 200 and 250 g were used in this study.

Anesthesia

All experiments were performed with the animals under general anesthesia. The anesthetic gas mixture was nitrous oxide 70%, oxygen 30% with halothane vapor 0—2.5%. The percentage of halothane was reduced during cooling and it was discontinued at 30°C. At lower temperatures anesthesia was maintained by cold narcosis. As cooling proceeded the oxygen concentration was rapidly increased to 100% so that the body fluids were saturated with this gas at the lower limit of hypothermia. The technique was reversed during warming.

Colling and Warning by Conduction

Surface cooling and warming were accomplished by spraying the upturned thorax and abdomen with water at the appropriate temperature. The apparatus consisted of a water reservoir and a spray driven by an electric pump. The animal's body was held in a small plastic box. This had a head recess for administering the anesthetic gases and an outlet pipe for returning the water to the reservoir. Water at 4°C was used for cooling and its temperature was maintained by adding ice. The ice-water was replaced by water at 40°C for surface warming. This temperature was maintained by a thermostatically controlled electric heating element located in the base of the reservoir.

Monitoring

The body temperature was recorded by rectal and mid-esophageal thermocouples during surface cooling and warming. The respiratory rate was counted by observing the chest movements and the heart rate was recorded by electrocardiography.

The Control Group of Rats

Twelve rats were cooled to 18°C and warmed to normal body temperature using the water spray. The cooling and warming times were recorded with the other parameters.

All other rats were cooled by the water spray and warmed by microwaves.

Microwave Warming

The apparatus was a 3 m × 1 m × 1 m cavity which was energized at a nominal frequency of 2.5 GHz by three water-cooled magnetrons. It contained a mode stirrer and a series of reflector plates which prevented the formation of static points of focal concentration in the random field of microwaves which was formed by reflection from its metallic interior. The magnetrons were each rated at 1.5 kW giving the cavity a dielectric heating power of 4.5 kW under optimal conditions. This heating power could be adjusted between zero and the maximum from a control console. The field in the center of the cavity was uniform in terms of its heating ability as shown by tests with a water load placed at different positions. This was the working area of the cavity and it contained a thin plastic staging for supporting the water jacket. The frequency of the microwaves corresponded to a free-space wavelength of 12.4 cm when measured with a coaxial wavemeter (Fig. 1).

The water jacket was made of plastic (Perspex). It was a vertical cylinder closed at the lower end by a 15 cm × 15 cm plate. This plate was supported at the corners by legs which were 3 cm high. The cylinder was 32 cm in height and it had an internal diameter of 6.5 cm. Compressed air was piped through the base to ensure gentle agitation of the water during exposure. The immersed rat was prevented from drowning by enclosing the head in a cylindrical plastic helmet. The anesthetic gases were piped through the upper surface of the helmet and they escaped from its lower border to the surface of the water. The rat's head was secured within the helmet by a collar. This was a circular disc with a slot cut away for the neck. The collar was fixed to the base of the helmet by a screw ring (Fig. 2).

Hypothermic rats were warmed from 18°C to determine the exposure time which would raise the body temperature to 38°C with the apparatus working at full power. During these observations the initial water jacket temperature was varied to determine the value which would ensure a water temperature of 40°C at the end of the exposure. This was repeated with the apparatus working at two thirds and one third of the power.

When these values had heen obtained three groups of twelve rats were warmed from 18°C to 38°C, one group for each power setting. The condition of the rats following

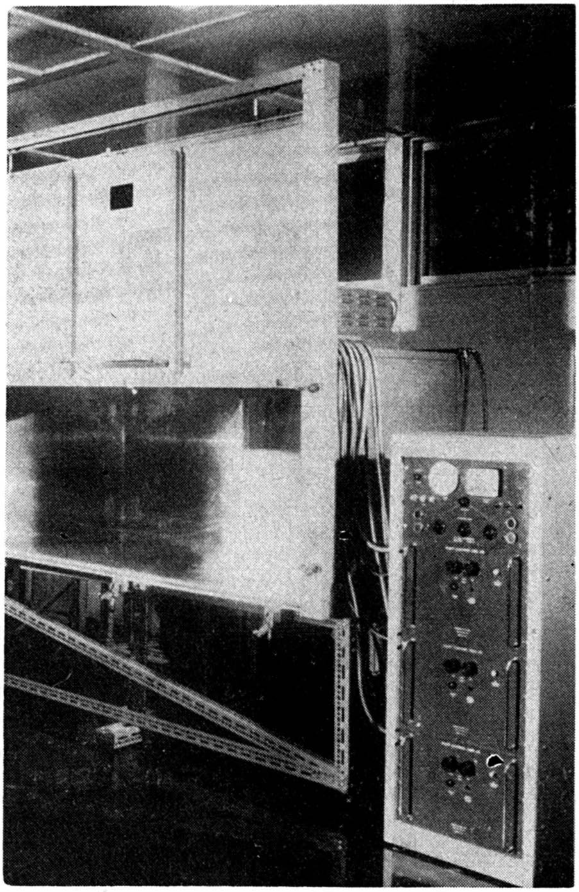

Fig. 1. The M. H. 1500 Microwave Cavity and Control Console. Original design of this experimental model by Elliot Electronics: England. One magnetron housing is seen on the top of the cavity behind the sliding door. The mode stirrer is located in the roof of the cavity behind the lower edge of the sliding door.

warming was observed. Damaged survivors were destroyed. The remaining survivors were allowed to recover from the anesthetic and they were returned to their cages for observation. Where minor burns became apparent after a delay, these animals were also destroyed. The others were maintained for three months before being subjected to post mortem examination.

Variations in the temperatures of the body tissues were studied in two rats following microwave warming from 18°C. One of the animals was killed before warming to eliminate circulatory effects. The tissues were probed with a thermocouple needle immediately after warming and again after a delay of two minutes.

Finally one rat was killed and skinned. The outline of the skin was traced on graph paper so that an estimate of the animal's surface area could be made for power calculations.

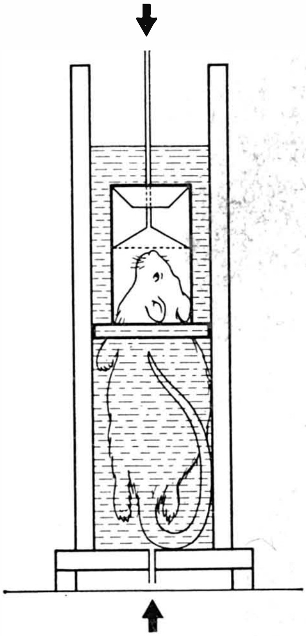

Fig. 2. The Perspex water jacket with the rat and helmet. The lower arrow indicates the inlet for the piped air supply. The upper arrow indicates the inlet for the anesthetic gases.

RESULTS

The twelve rats of the control group (those cooled and warmed by the water spray) all survived. The mean cooling time was 20 minutes and the mean warming time was 30 minutes (Fig. 3).

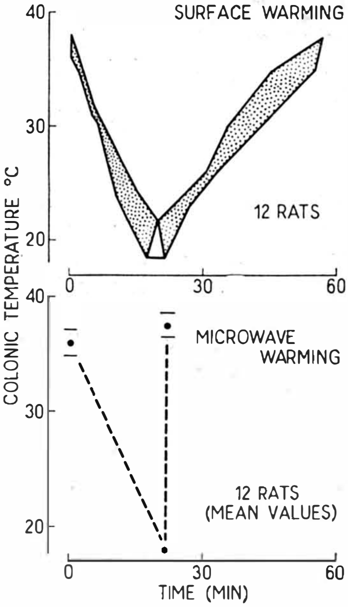

Fig. 3. The cooling and warming graphs of body temperature with time. The horizontal dashes bordering the pre-cooling and post--warming temperatures enclose two standard deviations.

The preliminary experiments with microwave warming indicated that a 20-second exposure was required to raise the body temperature of a 220 g rat from 18°C to 38°C when the apparatus was working at full power. The exposure time for warming through this range was shown to be inversely proportional to the power setting. Accordingly the exposure time required for warming at $^1/_3$ power was 60 seconds.

The volume of water required to cover the upper surface of the helmet with an adequate safety margin was in the region of 420—430 ml when the rat weight was approximately 220 g. This volume varied slightly according to the position adopted by the body. The initial water temperature needed to be no higher than 14°C to ensure that it did not exceed 40°C at the end of exposure.

The recordings of the heart rate and the respiratory rate were used for estimating the clinical state of the animal during cooling and warming. The measurements were obviously restricted to the pre- and post-warming periods where microwave warming was used. The values varied considerably with the level of hypothermia and the depth of anesthesia. In general the heart rate fell from the region of 420/minute to 100/minute during cooling. Similarly the respiratory rate fell from 100/minute to 10—20/minute. The heart rate and respiratory rate were if anything slightly faster than normal after warming by both methods.

The rectal and mid-esophageal temperatures did not differ significantly.

There were three deaths during microwave warming in the group of twelve rats warmed in the apparatus at full power. Two of the survivors developed superficial burns of the rump and they were destroyed.

Two deaths occurred in the group of twelve rats warmed at $^2/_3$ of the power. There were no obvious detrimental effects of microwave warming in the survivors.

All deaths during warming were due to cardio-respiratory failure as there was no evidence of thermal damage at post mortem.

All twelve rats warmed at $^1/_3$ of the power survived unharmed. This was cosidered to be the successful group. Accordingly this warming rate of 20°C in 60 seconds was considered to be the safe limit of microwave warming under the experimental conditions. For this reason the comparison of microwave warming with conventional conduction warming was restricted to this group (Fig. 3, Tab. 1).

During the three month period of observation all the undamaged survivors behaved in a normal manner. Several litters were produced and the offspring were bred through two generations. No specific studies were made on these animals but their apparent

Table 1

The mean values of results for rats warmed from 18°C to 38°C using $^1/_3$ of the rated power of the cavity. Standard Deviations in parenthesis.

Body Weight	216 g	(15 g)
Initial Temperature	36°C	(1°C)
Hypothermic Temperature	17.8°C	(0.5°C)
Cooling Time	21 min	(2.4 min)
Post Warming Temperature	37.7°C	(1.2°C)
Rise in Body Temperature	19.9°C	(1.3°C)
Volume of Water in Jacket	428 ml	(4.6 ml)
Initial Water Temperature	14.4°C	(0.3°C)
Final Water Temperature	39.8°C	(1.4°C)
Rise in Water Temperature	25.7°C	(1.2°C)
Exposure Time	60 s	

Table 2

Variations in tissue temperature following microwave warming. Rat one killed before warming. First temperature reading made immediately after warming. Second temperature reading made two minutes after warming.

Tissue	Rat One Readings °C Ist	Rat One Readings °C 2nd	Rat Two Readings °C Ist	Rat Two Readings °C 2nd
Skin	37	36	34	34
Liver	39	38	38	37
Large Intestine	36	37	34	28
Small Intestine	37	36	33	32
Kidney	39	38	38	36
Stomach	38	37	37	36
Lungs	35	35	37	36
Heart	38	37	36	36

normality was remarkable in view of the physiological stress suffered by their antecedents.

The variations in tissue temperature following microwave warming were virtually unaffected by the state of the circulation or a delay in making the measurements (Tab. 2).

The surface area of the 216 g rat was estimated to be 225 cm^2.

DISCUSSION

Safe microwave warming from 18°C to 38°C was achieved under the experimental conditions. This was twenty times faster than conventional surface warming. The experiments indicated that the physiological stress of rapid warming was well tolerated by the rat.

The division of power during microwave warming was calculated from the results. The mean rat weight, 216 g, was raised through 20°C in 60 seconds. The specific heat of the body was assumed to be 0.83 (5) and 1 kW was represented as 239 cal/s. The calculation indicated that power dissipation in the rat was at a rate of 0.25 kW. The mean water volume was 428 ml and this was raised through 27° C. Accordingly, power was dissipated in the water surrounding the rat at a rate of 0.75 kW. These were the figures with the cavity working at one third of its rated power. Inefficient coupling of the microwave field to the dielectric load, heat loss and power dissipation in the plastic accessories were thought to account for the remaining 0.5 kW.

It was impossible to measure the field strength of the microwaves in terms of mW/cm^2 for comparison with other studies where biological materials were exposed to beamed microwaves in free space. However it was desirable to make some estimate in these terms in view of the popular interest in the biological hazards of microwaves and safety standards for this type of electromagnetic energy.

One may suggest that the non-reflected part of the field incident on the animal had a power density which was functionally equivalent to 1100 mW/cm^2 as the estimated surface area of the 216 g rat was 225 cm^2.

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MAIN DIRECTIONS AND RESULTS OF RESEARCH CONDUCTED IN THE USSR ON THE BIOLOGIC EFFECTS OF MICROWAVES

Z.V. Gordon, A.V. Roščin and M.S. Byčkov

Labor Order of the Red Banner Institute for Scientific Research on Industrial Hygiene and Occupational Diseases, Academy of Medical Sciences of the USSR, Moscow, USSR

The research programe in the USSR uses three approaches, i.e., hygienic, clinical and experimental studies, directed to the investigating the biologic effects of a whole range of radiofrequencies, and particularly of microwaves which constitute the most biologically active part of the radiofrequency spectrum.

In the field of hygiene we have studied the working conditions accompanying various processes of production, from the development and building of a prototype to its serial production, then the conditions of daily performance and, finally, servicing and research work.

With the accumulation of hygienic, experimental and clinical data it became apparent that more strict assessment of occupational conditions is necessary for those working with microwave sources, including recording of the actual irradiation of the people, and particularly combination of microwave irradiation with other factors in the environment (soft X-rays, heat) which will be dealt with in the paper by Dr. K. V. Nikonova later during this meeting, as well as the mode of irradiation.

As our investigations have shown, the regime of microwave irradiation to which the workers are exposed has a pronounced intermittent character. While one group of activities is characterized by relatively or absolutely constant levels of irradiation (Fig. 1), in the other irradiation is changeable both in its intensity and time-course (duration of irradiation periods and of intervals between them, Fig. 2). From the statistical point of view, the actual exposure levels of those regulating microwave radio sets are subject to haphazard fluctuations, and therefore for the analysis of the irradiation data use was made of the appropriate theory of random processes.

The characteristics of random processes, such as statistical probability, dispersion and correlation functions, have shown that the random process under investigation is not a static one.

The results obtained determined our approach to hygienic studies in factories and

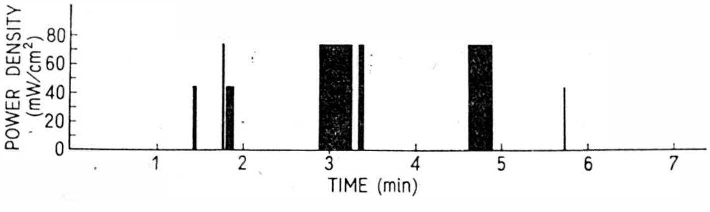


Fig. 1. Exposure to irradiation with two intermittent parameters, the duration of the irradiation periods and the intervals which separate them, the intensity of irradiation being relatively constant.

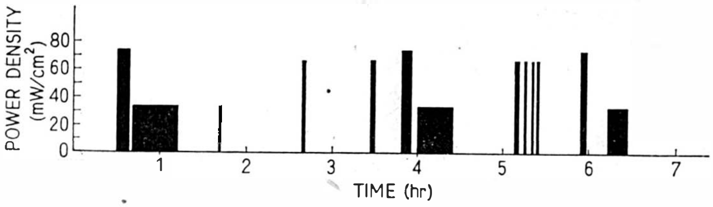


Fig. 2. The regime of irradiation in which both the intensity and the time parameters (the duration of irradiation periods and the intervals between them) have intermittent character.

led to the requirement for graphic recording of intensity and duration of irradiation during working shifts.

It has been possible to define some of the factors which influence to various degrees the characteristics of the irradiation process: number of radiation sources, particular design features of radiosets in production, sequence of technological steps, and many others.

Previous investigations conducted in our laboratory, coupled with evaluation of basic aspects of the biologic action of microwaves, made it possible to elucidate the importance of intermittent exposure factors for the biological effects of microwaves.

We used an experimental model of intermittent irradiation based on actual regimes of irradiation accompanying production. We found that, according to a number of indicators (fluctuations in weight and blood pressure, electroencephalography and electromyography, neurosecretory activity of hypothalamic nuclei), intermittent exposure to irradiation results in more pronounced biologic effects than those of steady irradiation under conditions of equal strength and time parameters. One could hypothesize that intermittent exposure is much more strenuous for the adaptation and compensation mechanisms owing to the frequent changes in the irradiation parameters.

Without dwelling upon the clinical direction of research, to which a separate paper by Dr. M. N. Sadčikova is devoted, we will only note that clinico-hygienic correlations made it possible to link the clinical indicators with intensity of microwave irradiation under industrial conditions. This unique material accumulated as a result of 20 years' observations made it possible to establish a very important fact, namely, that the biologic effects become more severe with increasing duration of work accompanied by irradiation of low intensities (less than 1 mW/cm^2).

Before going into experimental research, it is necessary to define certain terms which are frequently treated ambiguously. These are thermal and non-thermal effects.

Thermal effects are those biologic suquelae which are due to integral rise of temperature of the body and its separate parts during whole body or local irradiation.

Thermal effects are those biologic sequelae which are due to integral rise are the result of uneven heating of microstructures of a heterogeneous biologic tissue and may occur in the absence of the integral thermal effect. Finally, non-thermal or "extrathermal" effects are due to conversion of electromagnetic energy within an object into another form of non-thermal energy (molecular resonance absorption, photochemical reaction, etc.).

The present lack of adequate methods for separating nonthermal from thermoselective effects is the sole reason for their being put together under the provisional name of "non-thermal" effects.

The occurrence of pronounced biologic effects of microwaves of intensities which do not evoke the integral heat effect (less than 10 mW/cm^2) has been convincingly shown independently by a number of Soviet and foreign authors. Although there are differences of opinion on the "non-thermal" or "microthermal" nature of the biologic effects of low levels of energy, there should be no doubt at present as to the actual existence of these effects.

From this perspective, the studies on biologic effects of microwaves carried out 20 years ago in the USSR concerned high intensities (8, 25) and were limited only to establishing the minimal lethal doses, thermal action and some other effects (Tab. 1).

Table 1

Changes induced by microwave irradiation of high intensity (data of Belova, Gordon and Lobanova)

Investigated indicators	Radiation intensity (mW/cm²)	Duration of life or exposure	Character of the changes
1. 50% lethality, 10 cm band (rats)	100	15 min	Marked symptoms of overheating. Morphologically in the internal organs and nervous system significant vascular disturbances; slight evidence of dystrophic changes
2. Cataract formation (rabbits)	10	60 min	Opacity of the lens after 7 h irradiation
3. Thermal reaction (rats)	10	15—30—60 min	Maximal intensity which does not lead to elevated body temperature
4. Blood pressure (rats)	100	6—12 weeks 10 min each time	Lowered arterial pressure

The investigations were performed primarily at the levels of intensity which do not result in the integral thermal effect (less than 10 mW/cm²). The results obtained can be arranged provisionally into two groups: one presents the phenomenology of effects at various levels of life activities, while in the other various mechanisms of action are dealt with.

The phenomenology of the biologic effects of microwaves has been studied in most detail. Particular attention has been paid to the nervous system, as it is most sensitive (8, 22) and plays a key role in the pathogenesis of radiation sickness (8, 24, 29).

Some of the biologic effects resulting from microwave irradiation of non-thermogenic intensities are shown in Table 2 (only statistically significant results are quoted).

It can be seen that microwave radiation (intensity, 10 mW/cm²), when acting for long periods of time, constitutes a pathogenic factor (morphologic lesions in the nervous system, changes in reproductive function and some borderline conditions). The interpretation of these borderline conditions is equivocal and they cannot be confidently regarded as purely regulatory or adaptive and compensatory reactions which would be practically harmless. The include such effects as lowered endurance, retarded weight gain, inhibition of conditioned reflexes and neurosecretion, neurophysiologic disturbances.

However, irradiation that is lower in intensity by one order of magnitude (1 mW/cm²) is also significant from the medical point of view according to a number of indicators.

Table 2

Changes in certain functions of the organism of animals irradiated with microwaves of nonthermogenic intensity

Investigated functions	Radiation intensity (mW/cm²)	Type of experiment	Duration of each irradiation (min)	Animal species	Character of the changes
I. *General indicators*					
1. Endurance to effort — swimming	10	chronic	90	rats	decrease
2. Weight	10	chronic 4—8 weeks	60	rats	retarded weight gain
II. *Nervous system*					
1. Examination of electric activity of various brain structures by means of macro- and microelectrodes and stereotaxic technique (Byčkov, Dronov)	0.03—10	acute chronic	30—40 30—60	rabbits cats rabbits	predominantly generalized inactivation of the brain, domination of hypothalamic function; dissociation of integration of specific and nonspecific afferent systems at the thalamo-cortical level
2. Examination of behavioral reactions (Lobanova, Kicovskaja, 1968; Asabaev, 1970)	10 1	chronic (1—2 weeks) chronic (12—16 weeks)	60 60	rats mice birds	inhibition of conditioned reflexes, lowered excitability, weakening of the processes of stimulation and inhibition, increased spontaneous motor activity
3. Neuropharmacologic investigations (Kicovskaja, 1968; Zenina, 1964)	10	chronic (10 weeks)	60	rats rabbits	application of camphor, strychnine, nicotine and other neurotropic substances revealed lowered excitability of the motor zone of the cortex, subcortical structures and sensitive centers in the spinal cord with dissociation of the sensorimotor mechanisms at the spinal level

Tab. 2

Investigated functions	Radiation intensity (mW/cm^2)	Type of experiment	Duration of each irradiation (min)	Animal species	Character of the changes
4. Morphological changes in the nervous system (Tolgskaja, Gordon 1971)	10	chronic (8—25 weeks)	60	rats	changes in interneuronal axodendritic and axosomatic structures of the brain, and sensory nerves and receptors of various internal organs and the skin
5. Changes in neurosecretory function of the hypothalamus (Tolgskaja, Gordon 1968, 1971)	10	chronic (4—14 weeks)	60	rats	morphological and histochemical changes in secretory nuclei of the hypothalamus anterior suggesting inhibition of anterior activity
		chronic (20—26 weaks)	60		
III. *Cardiovascular system*					
1. Blood pressure	10	chronic (18—20 weeks)	60	rats	lowered arterial pressure
	1	chronic (12—14 weeks)	60	rats	
2. Chronotropic effect (Presman 1968)	1—10	—	20	rabbits	bradycardia or tachycardia
IV. *Biochemical changes*					
1. Cholinesterase					
— in the blood serum	10	chronic (20 weeks)	60	rabbits	lowered activity
— in the brain stem		(13 weeks)	60	rats	
— in the liver and heart (Nikogosjan 1960, 1964)		(23 weeks)	60	rats	

Tab. 2

Investigated functions	Radiation intensity (mW/cm²)	Type of experiment	Duration of each irradiation (min)	Animal species	Character of the changes
2. Catalase in blood (Nikogosjan 1960, 1964)	10	chronic (3 weeks)	60	rabbits	lowered activity
3. Acetylcholine					
— in the brain hemispheres	10	chronic (5 weeks)	60	rats	increased content
— in the brain stem	10	chronic (1 week)	60	rats	increased content
4. Histamine in the blood (Gelfon, 1964)	10	chronic (0.5 week)	60	rabbits	increased content
5. Aminoacid metabolism					
— protein fractions in the serum	10	chronic (20 weeks)	60	rabbits	increased content of albumins, decreased content of α, β and γ-globulins
— nonprotein nitrogen in the blood	10	chronic (20 weeks)	60	rats	increase in nonprotein nitrogen
— aminoacids in the urine	10	chronic (20 weeks)	60	rats	increased content
6. RNA (in the organs)					
— spleen	10	chronic (7—10 weeks)	60	rabbits	increased content
— brain and liver (Nikogosjan, 1964 a, b and c)	10	chronic (13 weeks)	60	rabbits	
7. Ascorbic acid (Nikogosjan, 1968)	10	chronic (22 weeks)	60	rabbits	increased content

Tab. 2

Investigated functions	Radiation intensity (mW/cm²)	Type of experiment	Duration of each irradiation (min)	Animal species	Character of the changes
V. *Reproductive function*					
1. Effects on gonads	10	chronic (20 weeks)	120	mice of both sexes	disturbances of the estrus cycle; changes in functional status of spermatozoids; slight evidence of degenerative changes in the gonads
2. Effects on fetal development	10	chronic (2.5—48 weeks)	120	mice	increased intrauterine lethality and frequent anomalies in fetal development
3. Effects on fertility	10	chronic (20 weeks)	120	mice (females)	decrease in number of successful crosses, reduced litter size
	10	chronic (20 weeks)	120	mice (males)	increased percentage of abnormal offspring
	10	chronic (48 weeks)	120	mice (females)	decreased number of gestations and births, inferiority of the offspring (particularly of the first and subsequent gestations), premature cessation of reproductive function
	0.250	chronic (48 weeks)	240	mice (females)	
	10	chronic (48 weeks)	120	mice (males)	decreased fecundity and litter size; premature cessation of reproductive function
	0.250	chronic	240		
VI. *Nonspecific reactivity*					
1. Immunologic effects	0.5	chronic (40 weeks)	60	rats	lovere natural resistance (inhibition of natural immunity)

Upon cessation of irradiation some of its sequelae may disappear but a prolonged action results in destructive, irreversible pathologic lesions.

Attention is drawn to the fact that, as can be seen in Table 2, even at intensities that are extremely low by comparison with those considered above (e.g., 500—250 μW/cm^2), certain biologic effects occur (bioelectric phenomena with resetting to a new level of activity of the brain systems, changes in immunobiologic resistance), including definite pathologic effects (reproductive functions).

When speaking about criteria of significance of reactions, one should keep in mind that not all reactions are of importance but some, while lacking pathologic traits under certain conditions, should nevertheless be given attention when possible harmful consequences are considered. It is therefore necessary to introduce the term "potentially harmful reaction" as a main criterion of importance of a symptom, as opposed to either a threshold biologic (regulatory) reaction in general or a threshold pathologic reaction.

Studies of qualitative and quantitative indicators of the biologic action of microwaves have yielded data which not only allowed assessment of the biologic effects of microwave irradiation of various parameters but also showed main directions for research aimed at elucidation of a whole range of pathogenic mechanisms, from the molecular level up to system and intersystem relationships.

Our investigations of primary mechanisms of the biologic action of microwaves have been directed in particular towards studying the possibility of a direct action of microwaves upon the activity of some physiologically important enzymes (catalase, cholinesterase, actinomyosin). We have also tried to influence permeability of ions across cell membranes by microwave exposure.

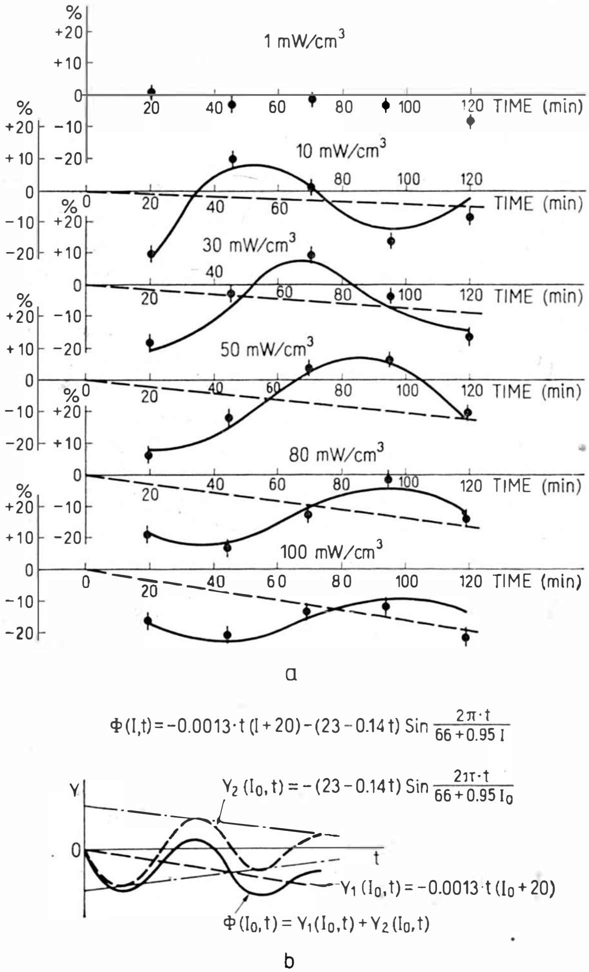
Studies on the influence of microwave irradiation of the range of 10 cm on catalase and cholinesterase activities *in vitro* using various conditions gave negative results. Attempts to demonstrate *in vitro* any direct influence of the field upon the enzyme molecules which would result in changes of enzymatic activity have failed. At the same time our *in vivo* investigations have shown that activity of a whole range of enzymes in the tissues of irradiated animals, including cholinesterase, changes markedly at intensities significantly lower (by at least one order of magnitude, down to 1 mW/cm^2) than those used in *in vitro* experiments (14, 15, 19, 30). It was possible to show, by means of a simple method and taking as an example nonspecific serum cholinesterase, that changes in tissue activity of the enzyme following whole body irradiation result not from a direct action on molecular structures but from changes in enzyme concentration in the tissues, apparently related to disturbances in the neurohormonal regulation of metabolic processes.

It has been possible to demonstrate a direct action of microwaves upon enzyme activity using preparations of rabbit muscle actinomyosin which possesses a more complex level of biologic organization than catalase and cholinesterase and is distinguished by a highly labile conformation. Irradiation of actinomyosin gel at 350 MHz frequency with the density of the absorbed energy of about 5 mW/cm^2 resulted a reduction in ATP-ase activity.

In another series of biophysical investigations the influence of microwaves upon cell membranes was studied, and particularly on their selective permeability to the ions which influence the membrane electric potential, K+ and Na+. Isolated human blood erythrocytes provided the biologic model for studies of microwave influence on membrane permeability. Changes in influx rates of radiolabelled K^+ and Na^+ into red blood cells were determined during and after microwave irradiation within the dose range of 900 to 2340 MHz, and compared with respective heat controls. Relationships between irradiation parameters (frequency, intensity and duration) and changes in ion transport into erythrocytes were investigated.

The results revealed statistically significant changes in the rates of transport of K^+ and Na^+ ions across membranes not related to a rise in temperature of the suspension. These changes did not depend on radiation frequency within the range investigated (31, 32). The threshold microwave intensity leading to a significant change in the rates of ion transport following irradiation for two hours approximated 1 mW/cm². The relationship between intensity and duration of irradiation and its effects was of a multiphasic character and did not follow a linear dose-effect relationship with regard to absorbed energy.

The above experimental data were used to develop a mathematical model showing how changes in K^+ influx rate depend on intensity and duration of irradiation. Within



$$\Phi(I,t) = -0.0013\cdot t\,(I+20) - (23-0.14t)\,\mathrm{Sin}\,\frac{2\pi\cdot t}{66+0.95\,I}$$

$$Y_2(I_0,t) = -(23-0.14t)\,\mathrm{Sin}\,\frac{2\pi\cdot t}{66+0.95\,I_0}$$

$$Y_1(I_0,t) = -0.0013\cdot t\,(I_0+20)$$

$$\Phi(I_0,t) = Y_1(I_0,t) + Y_2(I_0,t)$$

Fig. 3 a. The dependence of changes in the rate of entry of potassium into erythrocytes upon duration of irradiation at fixed intensities. The solid lines show the estimated functions of the dependence of effect on the time of irradiation, as obtained from a mathematical model of the process. The broken lines represent the linear component. b. The graphic and analytical presentations of the process as a resultant of two components.

the constraints of the model, the observed effect is interpreted as a resultant of two processes: linear decline in K^+ entry rate with increasing dose of absorbed energy and change of the rate of transport under conditions of diminishing adaptation possibility (Fig. 3 a and b). These processes account for the multiphasic oscillatory character of the effect during the course of the experiment.

It is important to emphasize that even in such relatively simple objects as erythrocytes, the regulatory processes contribute significantly to the ultimate biologic effect (changes in the rate of ion transport). Indeed, it has been shown that the primary effect, depending linearly on the dose of energy, has a triggering effect on cell regulatory phenomena. The overlapping of regulatory processes and the primary effect determines the complex, non-linear character of the relationship between intensity and duration of irradiation (i.e., the dose of energy) and biologic effects. It appears that it is even more so when we deal with reactions of much more complex systems, such as the whole organism, to irradiation of relatively low intensity, or prolonged exposure at intensities which do not evoke pathologic lesions during short-term exposures. In such cases external evidence of the biologic effects is limited, as a rule, to reflections of changes in complex regulatory processes, only indirectly connected with the action of electromagnetic energy. This is presumably why, particularly within the range of low intensities (up to 10 mW/cm^2), it proves impossible to obtain a simple quantitative relationship between intensity and duration of irradiation, on the one hand, and the biologic effect on the other. It has been shown (3) that, apart from the depolarizing action of microwaves upon excitable membranes, hyperpolarizing effects occur (rise in membrane potential of muscle fibres).

Electrophysiologic investigations of elementary excitable structures (3) at an extremely low intensity of irradiation (5 $\mu W/cm^2$) have revealed changes in a number of functional parameters and characteristics, namely, a slowed conduction of impulses, an increased synaptic delay, lengthening of latent and refractory periods, changes in action potential (all in isolated nerve and muscle fibres of the frog), inhibition of the impulse

Table 3

Changes in the amplitude of action potentials (stimulation frequency, 20 Hz), optimal and maximal rhythms of the frog muscle fibre

	Amplitude of action potentials			Optimal rhythms			Maximal rhythms		
	Arithmetic means and ranges of variation in % of the initial value	p in comparison with control	Criterion of significance	Arithmetic means and ranges of variation in % of the initial value	p in comparison with control	Criterion of significance	Arithmetic means and ranges of variation in % of the initial value	p in comparison with control	Criterion of significance
Control group	100 (99—103)			10			20		
Experimental group	79 (51—-86)	< 0.01	Wilcoxon's	58	0.025	Fisher's	84	< 0.025	Fisher's

Table 4

Changes in the rate of conduction of impulses and absolute refractory period in the frog muscle fiber

Group	Rate of conduction			Refractory period		
	Arithmetic means and ranges of variation in % of the initial value	p in comparison with control	Criterion of significance	Arithmetic means and ranges of variation in % of the initial value	p in comparison with control	Criterion of significance
Control	100 (98—102)	0.01		99 (97—102)		
Experimental	75 (64—85)	0.01	Wilcoxon's	150 (94—176)	0.05	Wilcoxon's

activity of single ganglionic neurons (the medicinal leech). Some of these results are presented in Tables 3 to 5.

Table 5

Changes in synaptic delay (myoneural transmission in the frog)

Group	Arithmetic means and ranges of variation in % of the initial value	p in comparison with control	Criterion of significance
Control	103 (90—110)		
Experimental	140 (100—167)	< 0.01	Wilcoxon's

Results of studies on red blood cell membranes coupled with data on the influence of microwave irradiation on isolated excitable structures (2, 6, 9, 10, 13, 32) make it possible to hypothesize that the influence of microwaves on excitable cells is connected with alterations in the permeability of the cell membranes brought about by changes in transport of ions, which influence the membrane potential.

Unfortunately, we do not have at present data on the precise physicochemical nature of the processes leading to changes in ion transport across membranes of the irradiated cells. Undoubtedly, these processes would be worth studying in greater detail.

Consideration of the possibility of a selective absorption of microwave energy at interfaces of heterogeneous biologic systems led to the assumption that the single physical mechanism — a selective absorption of electromagnetic field energy at the surfaces of colloid molecules, membranes and other cell constituents — underlies the various "non-thermal" biologic effects of electromagnetic fields. This may be true since the surface conductivity is increased within the double electric layer at the interfaces of biologic objects. Biophysical studies aiming at experimental testing of this assumption are being planned.

Finally, at the system and organism levels, particular attention has been paid to the mechanisms of biologic effects in the central nervous system. As a result of neurophysiologic investigations, CNS effects have been observed at intensities up to 1 mW/cm^2. These effects are determined by both a direct action on the brain and the reflex component and intersystem relations within the brain (3, 4, 5).

Particularly interesting in the pathogenesis of radiation sickness are the intersystem relations. These include processes in such systems as a) the reticular formation of the brain stem, the hypothalamus and the cortex of the cerebral hemispheres and b) the cortex and thalamus.

Changes in the nervous system are characterized first of all by a marked contribution from nonspecific subcortical and stem structures superimposed upon cortex effects. This is particularly true of the hypothalamus, where changes at low intensities (30—100 μW//cm^2), taking place in both acute and chronic experiments, are of exceptional interest because the hypothalamus constitutes the structure connecting nervous and humoral means of regulation (hypothalamic — hypophyseal — suprarenal system).

The most characteristic syndrome shown by the system reticular formation of the brain stem — hypothalamus — cortex is the syndrome of generalized inactivation (Fig. 4). Disruption of the integrating activities of the specific and nonspecific afferent systems of the brain (thalamo-cortico-thalamic cycle) takes place simultaneously. Experimental investigations (11, 12) show that, following microwave irradiation, the ascending activating influence of the reticular formation on the brain cortex is blocked.

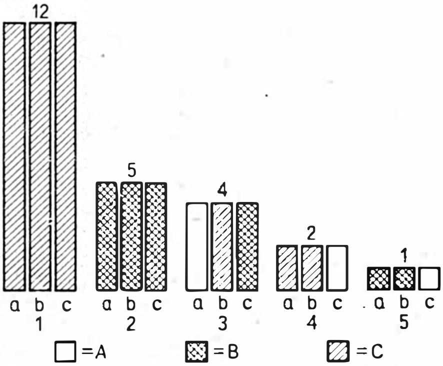


Fig. 4. The variants of relations between shifts in the cortex of hemispheres, posterior hypothalamus and reticular formation of the brain stem accompanying the exposure to SHF fields. The numbers at the top indicate the number of rabbits demonstrating a given effect. The numbers at the bottom correspond to sequential numbers of the variants. Symbols: *A* — Lack of effect of SHF, *B* — Activation, *C* — Deactivation, *a* — The cortex of hemispheres, *b* — Posterior hypothalamus, *c* — The reticular formation of the brain stem.

Changes in the regulatory activities of the hypothalamic region due to microwave irradiation of nonthermogenic intensities also result in shifts in cholinergic processes (19, 26), participation of choline-reactive (5, 11) and adrenergic (5) structures of the brain, as well as biphasic changes in vascular tonus (8, 25) with accompanying changes in accumulation of neurosecretion within the nervous cells and tissues of the hypothalamic region (27, 28).

At low intensities (of the order of 1 mW/cm^2) microwave-induced disturbances of adaptation to various factors have also been observed (25).

All the above findings taken together bring us closer to understanding the pathogenesis of the neurologic manifestations of microwave sickness by showing clearly that in human beings the astheno-vegetative shifts and psychophysiologic symptoms are mainly of a mesencephalo-diencephalic nature, and are elicited by microwave action of low intensity.

The program of further investigations envisages elucidation of new aspects of the mechanism of biologic action of microwaves, of late sequelae of this action, and of the restoration period. Particular attention will be paid to the combined action of microwaves and other physical factors of the working environment, various exposure conditions, threshold significance of biologic effects depending upon wave-range and modulation characteristics, and the reliability of forecasting of possible harmful effects.

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PHARMACOLOGIC EFFECTS OF A PULSED MICROWAVE FIELD

B. Servantie, G. Bertharion*, R. Joly*, A. M. Servantie,*
J. Etienne, P. Dreyfus and P. Escoubet

Postgraduate School of the Navy Medical Service; Center of Biophysiologic Studies and Research Applied to the Navy; Military Hospital for Postgraduate Study, Sainte Anne, Toulon — Naval, France

For a few years, we have been studying the effects of prolonged microwave exposures of laboratory animals. Systematically, we used low mean power densities, looking for biologic effects which are not obviously of thermal origin. Our aim is to present certain pharmacologic observations made by us.

DESCRIPTION OF THE EQUIPMENT**

1. **Generators.** We have used navy generators, which are more fitted for biologic research. These generators produced a pulsed hyperfrequency field of 10 cm wavelength (S band: 3000 MHz) with a maximum peak power of 600 kW. The pulse duration is 1 microsecond, variable between 0.9 and 1.2 μs depending on the magnetron used, with a pulse repetition rate of 525 Hz, variable between 450 and 650. The maximum mean power is consequently 350 W. Usually we employed long-term exposures of many weeks, sometimes many months. Two identical generators which can be exchanged were used.
2. **Anechoic chamber.** The emitted field was transmitted through a wave guide to a 15 dB horn. This horn was fixed on the wall of a 20 m^3 anechoic chamber in which animals could be irradiated in free space and far field conditions; the experimental subjects, in specially designed Plexiglass cages, were placed at more than two meters from the horn, the Rayleigh distance being of one meter; in the exposure region, the mean power density, measured in the absence of animals, was 5 ± 1 mW/cm^2.
3. **Measurements.** Power densities were measured by means of a Hewlett-Packard 432 A milliwatt-meter connected to a 478 A thermistor mount. To determine frequencies (except hyperfrequency) and duration, we used a Hewlett-Packard 5326 B timer-counter. Our measurements were made either directly at the generator output by a coupler-attenuator, or in the anechoic chamber with a tuned dipole or a calibrated horn.

FIELD EFFECT ON SENSITIVITY TO PENTETRAZOL

1. **Techniques.** Our experiments were carried out on 300 albino CD-1 mice of the Charles River strain; the body weight ranged between 30 and 35 g. Experimental and control groups were selected at random, in equal numbers.

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* Military Medical Corps.

** We thank the Office for Research and Experimental Facilities (D.R.M.E., French Ministry of Defence) for its assistance.

The experimental animals were exposed to microwaves for periods of 8, 15, 20, 27 and 36 days, according to the above-described conditions. Normal mice were maintained under the same environmental conditions, outside the anechoic chamber. Each experiment was repeated three times.

At the end of the exposure period, 50 mg/kg of pentetrazol were administered intraperitoneally to each mouse; the time interval from the injection to the beginning of the convulsive fit was measured. At the end of each experiment the mortality of the mice was determined.

2. **Results.** It was found that exposures to microwave fields affected the convulsion times and the mortality.

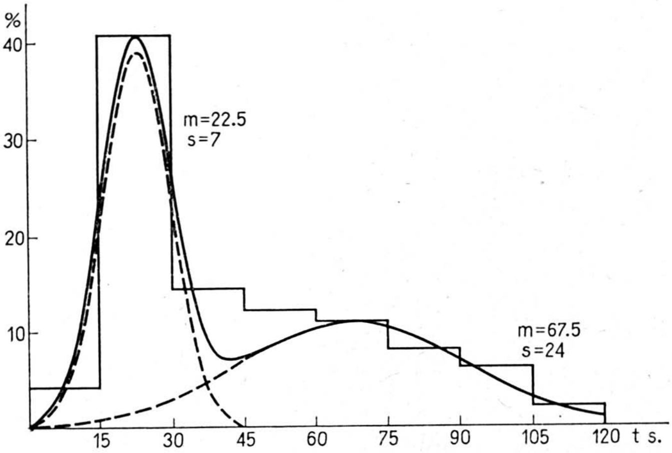

Fig. 1. Pentetrazol convulsion times — controls.

Table 1

Pentetrazol convulsion time ratios

Exposure times	Less susceptible / More susceptible	Experimental / Controls
Controls	1.13	—
8 days	1.29	1.14
15 days	0.64	0.56
20 days	1.66	1.47
27 days	1.81	1.60
36 days	1.44	1.27

a. **Convulsion times.** Histograms of the time intervals between the injection and the beginning of the fit were drawn for each experimental and control group. There is no statistically significant difference between the various control groups; we can treat them together as one normal population (see Fig. 1). As a matter of fact, this normal population can be assigned a sum of two gaussian distributions, with a probability ranging between 0.99 and 0.975. The parameters (mean and standard deviation) of these two distributions were: 22.5 s and 7 s for the first, 67.5 s and 24 s for the second.

This represents a good approximation to the distribution of the convulsion times for normal mice, which vary from 7 to 120 seconds. Consequently, it appears that, in the strain of mice with which we have worked, there are animals which are more susceptible than others to the convulsive action of pentetrazol: the two types were represented in approximately equal numbers.

For irradiated mice, all groups, except the 8-day group, differ significantly from the control population. The individual groups were too small to permit calculation of the theoretical distribution; nevertheless, the "more susceptible" and "less susceptible" cate-

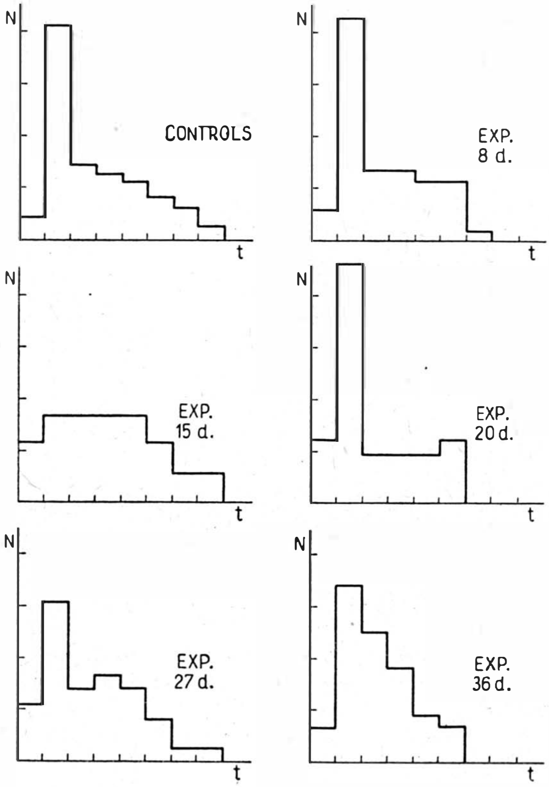

Fig. 2. Pentetrazol convulsion times.

Table 2

Pentetrazol percentage mortalities

Exposure times	Experimental animals	Normals
8 days	20.0	20.0
15 days	16.67	6.25
20 days	20.0	6.67
27 days	15.62	14.28
36 days	33.0	14.0

gories are found again on the histograms (see Fig. 2). It was assumed that a good evaluation of the microwave field action would be obtained from the ratio between these two categories. To compute this ratio, the time corresponding to the intersection of the two theoretical curves on Figure 1 (broken line) representing the distribution of convulsion times within the two theoretical normal populations, that is 36.75 seconds, was taken.

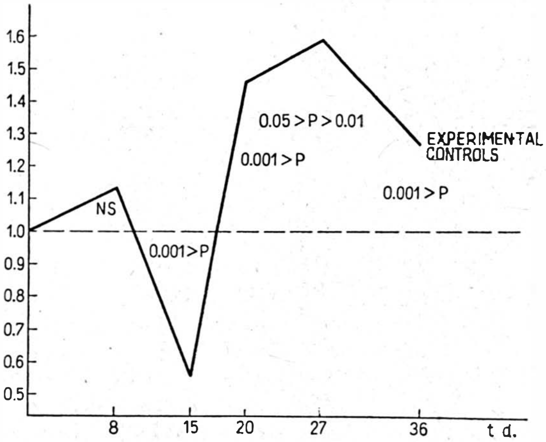

Fig. 3. Pentetrazol: ratio of "more susceptible" to "less susceptible" animals in the experimental groups as compared to the controls, as a function of exposure time.

The values obtained are summarized in Table 1. The convulsion time ratios for experimental animals compared to controls were plotted against exposure times (see Fig. 3): for 8 days' exposure, there was no difference between experimental and control groups; after 15 days, the number of "less susceptible" animals increased: the exposure to microwaves delays the appearance of the fit. For longer exposures, on the contrary, the number of "more susceptible" animals increases: the exposure to the fields tends to hasten the onset of the fit, particularly after 27 days of exposure.

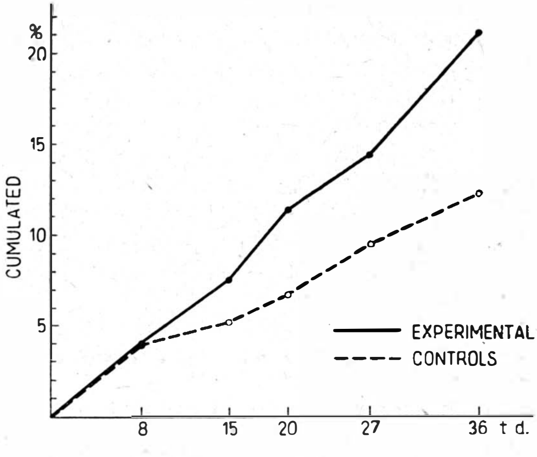

Fig. 4. Pentetrazol mortality.

b. **Mortality.** In each test, the animals which died after the fit were counted. The results are shown in Table 2, for control and experimental groups. There is a statistically significant difference (p between 0.005 and 0.001) between control and experimental populations. This difference is seen more clearly in Figure 4 with cumulated percentages plotted along the abscissae: it is non-exstent for the 8-day exposure, it appears for the 15-day exposure and increases for longer exposures.

Consequently it appears that in mice under our experimental conditions the effect of microwave exposure on convulsion times and mortality becomes perceptible only after a period longer than 8 days.

FIELD EFFECT ON SENSITIVITY TO CURARE-LIKE DRUGS

1. **Techniques.** To study the susceptibility of animals to curare-like drugs, we have used three different methods: Experiments on the intact animal, on an "*in situ*" neuromuscular preparation, and on an isolated neuromuscular preparation. All experimental animals were irradiated for 10 to 15 days: the control animals were held during the same time under the same environmental conditions.

a. **Intact animals:** 64 control and 78 experimental rats of the Charles River strain were used. In each rat, after anesthesia with Nembutal, a catheter was introduced into the jugular vein, following which the tested drug (Gallamin, suxamethonium) was injected at the rate of 1 mg/min; the time required for the disappearance of all movements, particularly respiratory movements was measured and from this we computed the amount in mg/kg necessary to obtain complete paralysis.

b. *In situ* preparation: 16 control and 24 experimental rats were used. In each rat, after anesthesia with Nembutal, a jugalar vein catheter, a tracheal cannula for assisted respiration and a rectal thermistor were introduced; the tendon of the left gastrocnemium muscle was set free, and then fastened to an isometric transducer which was connected to a paper recorder; the left sciatic nerve, after central tying, was stimulated by 6 volts 0.5 millisecond rectangular electric shocks with 0.1 Hz frequency; after a 10-minute waiting time for attainment of the steady state of the preparation, we gave a quick injection of 0.1 mg/kg of the tested drug (Pancuronium bromide); the amplitude in percentages of the initial value was computed from the recording.

c. **Isolated preparation.** 166 control and 166 experimental rats were used; each animal was decapitated without anesthesia; the left half of the diaphragm with the left phrenic nerve was taken out and placed in an oxygenated Tyrode bath at laboratory temperature; the nerve was stimulated by electric shocks identical with those of the *in situ* preparation; a glass pen fastened to the muscle recorded the twitches on a smoked drum; one normal and one experimental preparation were prepared simultaneously; after attaining a steady state, the tested drug (decamethonium: 146.3 μg/ml; suxamethonium: 3 μg/ml; tubocurarin: 3 μg/ml; diallylnortoxiferin; 5 μg/ml) was added to the bath and left undisturbed for three minutes; then the preparation was washed with uniform Tyrode flow of 4 000 ml/h for 10 minutes; the percentage decrease in amplitude per minute was computed from the recordings.

2. **Results.** All these experiments demonstrated that irradiated rats appear to be less susceptible to paralysing drugs than normal rats.

a. **Intact animal:** Table 3 shows a comparison between the numbers of animals which were paralysed by less than a threshold dose: 6 mg/kg for gallamin, 1.5 mg/kg for suxamethonium: there is a very significant difference (p lower than 0.001) between experimental and control animals, the former requiring higher doses for paralysis.

b. *In situ* **preparation:** the averaged curves from records were plotted (see Fig. 5) as for the intact animal technique; the experimental rats were paralysed to a lesser

Table 3

Gallamine — 6 mg/kg

	Control	Experimental animals
Paralysed rats	45	32
Non-paralysed rats	19	44
Total	64	76

($\chi^2 = 15.93$)
$p < 0.001$

Suxamethonium — 1.5 mg/kg

	Control	Experimental animals
Paralysed rats	21	6
Non-paralysed rats	6	18
Total	27	24

($\chi^2 = 12.17$)
$p < 0.001$

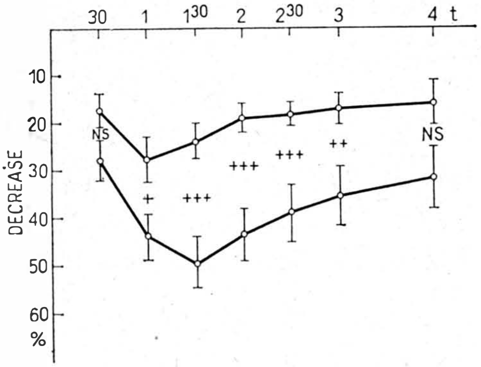

Fig. 5. Amplitude decrease after Pancuronium. NS = not significant; + = significant.

Table 4

Pancuronium

	30s	1 min	1 min 30 s	2 min	2 min 30 s	3 min	4 min
Difference %	10.65	16.53	25.6	24.8	21.12	18.44	15.92
t	1.94	2.38	4.08	4.35	3.54	2.76	1.80
	NS	$0.025 > P > 0.02$	$0.001 > P_o$	$0.001 > P_o$	$0.005 > P_o > 0.001$	$0.01 > P_o > 0.005$	NS

NS = not significant

extent than control rats. With this technique, we obtained an additional result: the recovery was faster for irradiated animals than for controls; the difference between the averaged curves, not statistically significant for 30 seconds, was very significant from 1 to 3 minutes (see Tab. 4).

c. **Isolated preparation**: four drugs were tested: two (decamethonium and suxamethonium) are leptocurares which stabilize the depolarization of the membrane, and two

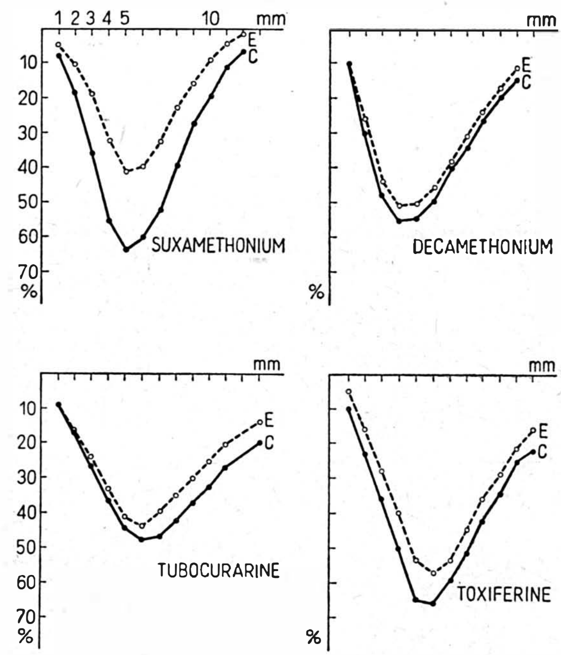

Fig. 6. Isolated preparations.

Table 5

Suxamethonium

		1	2	3	4	5	6	7	8	9	10	11	12
N	m	8.3 ±0.89	18.7 ±1.19	36.6 ±4.12	55.5 ±5.03	64.7 ±4.92	61.3 ±5.75	53.0 ±6.47	40.1 ±6.58	27.9 ±6.26	19.5 ±5.71	11.9 ±4.88	6.8 ±4.36
	n	19	19	19	19	19	19	19	19	19	18	18	18
E	m	4.7 ±0.58	10.6 ±1.13	19.2 ±2.12	33.2 ±3.50	41.7 ±5.06	40.3 ±5,82	33.0 ±5.91	23.1 ±5.30	16.3 ±4.50	9.4 ±3.74	4.6 ±3.24	1.6 ±2.70
	n	26	26	26	26	26	26	26	26	25	24	23	22
	d%	43.4	43.3	47.5	40.2	35.5	34.3	37.7	42.4	41.6	51.8	61.3	76.5
	t	3.53	4.85	4.06	3.77	3.17	2.50	2.26	2.03	1.54	1.53	1.29	1.06
		$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.005$	$P<0.02$	$P<0.05$	$P<0.05$	NS	NS	NS	NS

Table 6

Decamethonium

		1	2	3	4	5	6	7	8	9	10	11
N	m	10.3 ± 0.95	29.6 ± 1.68	27.7 ± 1.80	55.7 ± 1.77	54.9 1.86	49.5 ± 1.93	42.5 ± 2.03	34.4 ± 1.95	26.2 ± 2.02	19.5 ± 1.95	14.5 ± 1.80
	n	78	78	78	78	78	78	78	78	78	78	76
E	m	9.3 ± 0.82	26.6 ± 1.55	44.0 ± 1.96	51.5 ± 1.75	50.7 ± 1.76	46.1 ± 1.87	38.9 ± 2.08	30.9 ± 2.10	23.2 ± 1.91	17.0 ± 1.67	11.5 ± 1.49
	n	70	70	70	70	70	70	70	70	70	70	68
d%		9.7	10.1	7.8	7.5	6.7	6.9	8.5	10.2	11.5	12.8	20.7
t		0.79	1.31	1.39	1.68	1.63	1.26	1.24				
		NS	(P<0.2) NS	(P<0.2) NS	(P<0.1) NS	(P<0.1) NS	NS	NS	NS	NS	NS	NS

Table 7

Tubocurarine

		1	2	3	4	5	6	7	8	9	10	11	12	13
N	m	8.8 ± 0.57	17.6 ± 0.86	27.0 ± 1.32	37.1 ± 2.02	45.0 ± 2.35	48.5 ± 2.55	47.9 ± 2.58	43.3 ± 2.59	38.1 ± 2.72	33.2 ± 2.59	27.8 ± 2.47	24.0 ± 2.34	20.4 ± 2.26
	n	46	46	46	45	45	45	45	45	45	45	45	45	45
E	m	9.4	17.7	25.4	34.8	42.7	44.7	40.9	35.4	30.8	25.9	20.8	17.2	14.2
	n	45	45	45	44	44	44	44	44	44	44	44	44	44
d%		—6.8	—0.6	4.8	6.2	5.7	7.8	14.6	17.8	19.2	22.0	25.2	28.3	30.4
t		0.57	0.07	0.72	0.91	0.89	1.19	2.10	2.29	2.09	2.10	2.32	2.36	2.25
		NS	NS	NS	NS	NS	NS	$P<0.05$	$P<0.025$	$P<0.05$	$P<0.05$	$P<0.025$	$P<0.025$	$P<0.05$

others (tubocurarine and toxiferin) are pachycurares which stabilize the polarization of the membrane; for both kinds, the results (see Fig. 6 and Tab. 5, 6, 7, and 8) are similar: the preparations obtained from irradiated rats are paralysed to a lesser extent and recover sooner than those from normal rats; the difference is evident and very significant for suxamethonium and toxiferin; less evident or not significant for the two other drugs.

Table 8

Toxiferin

		1	2	3	4	5	6	7	8	9	10	11	12
N	m	9.6 ±0.88	23.2 ±2.14	37.1 ±3.24	52.7 ±4.01	65.6 ±4.13	66.8 ±4.00	60.2 ±4.30	52.1 ±4.62	42.3 ±4.47	34.4 ±4.55	27.7 ±4.61	22.4 ±4.44
	n	23	23	23	23	23	23	23	23	23	23	22	22
E	m	4.9 ±0.93	16.4 ±1.70	23.4 ±2.53	40.9 ±2.95	54.4 ±3.03	58.2 ±3.00	54.7 ±3.30	45.4 ±3.63	36.6 ±3.72	29.5 ±3.83	22.1 ±3.51	16.6 ±3.01
	n	25	25	25	25	25	25	25	25	25	24	24	24
d%		49.0	29.3	36.9	22.4	17.1	12.9	9.1	12.9	13.5	14.2	20.2	25.9
t		3.58	2.50	2.14	2.40	2.22	1.73	—	—	—	—	—	—
		$P<0.001$	$P<0.02$	$P<0.05$	$P<0.02$	$P<0.05$	NS	NS	NS	NS	NS	NS	NS

DISCUSSION

These results show that exposure to a microwave field of a 5 mW/cm^2 mean power density for a few days alters the susceptibility of animals to certain drugs.

Our experiments with pentetrazol were begun following our observations of the alterations in the rat EEG (2) following exposure to a microwave field; at that time, we were unaware of the work of Barański and Edelwejn (1). The EEG records of rats which we had irradiated with microwaves in the above-described conditions (2) showed alterations analogous to those which are found in an epileptic fit. We supposed that the susceptibility to a convulsant should be increased in a parallel way to EEG alterations, but Figure 3 shows a biphasic variation in susceptibility which cannot be explained at this time.

We were led to study the susceptibility to curare-like drugs by an accidental observation, also during our work on the EEG. Even more than our experiments with pentetrazol, these drugs have permitted us to begin to understand the way in which the microwave field acts.

Many hypotheses to explain a decrease in susceptibility to a drug could be advanced:

1) the absorption decreases;

2) the excretion is increased;

3) the distribution volume is increased, or modifications of the blood distribution occur;

4) the binding between the drug and the carrier protein increases;

5) the enzymatic mechanism is modified, either by a decrease in the quantity of the enzyme or by a modification in the enzyme itself.

Our experiments, and particularly the isolated diaphragm trials, lead us to localize the action of the field at the level of the neuromuscular synapse; consequently, we can exclude the first four hypotheses.

We have measured neuromuscular excitability, which is identical for normal and irradiated rats; we have also tried to titrate the enzyme acetylcholinesterase in the muscle without finding any difference between normal and irradiated animals.

For all these reasons, it seems to us that the microwave field, acting on the muscular level of the neuromuscular synapse, creates a decrease in the binding energy between the drug molecule and the enzyme molecule; such a decrease could explain the difference between the susceptibility to curare of normal and irradiated animals. We shall now try to check this hypothesis.

CONCLUSION

We have shown that albino rats, after a few days of exposure to a microwave field, do not react in the same way to certain drugs as normal animals do. For curare-like products, we can locate the site of action of the field at the neuromuscular synapse, and more precisely at the post-synaptic membrane; the mechanism is an alteration of the acetylcholinesterase molecule by the field, probably by a decrease of the binding energy.

It is unlikely that this mechanism is the only one by which a microwave field is able to act on living matter. Among the numerous biological effects of microwaves which are quoted in the literature, we shall certainly find many other mechanisms operative.

As a matter of fact, many of these biological effects of microwaves are probably parts of a "psychologic disease" which is not generally apparent by itself, but is revealed by some external agents.

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MICROWAVE IRRADIATION AND ENDOCRINE FUNCTIONS

H. J. Mikołajczyk

Institute of Occupational Medicine, Łódź, Poland

During investigations on the biologic effects of microwaves attention should be paid to the endocrine functions. This is because of the following reasons:

1. The transformation of electromagnetic energy into heat within living tissues justifies research on pituitary-thyroid functions because of the physiologic role of the thyroid hormones for heat production in the animal body.
2. Microwave irradiation can be an environmental stress factor and thus it is reasonable to investigate the pituitary-adrenocortical system because of its major importance in the stress reaction of the animal organism.
3. The function of male gonads shows a natural sensitivity to the harmful effect of excessive heating; this provides the logical background for studies of the pituitary-gonadal system in the case of microwave irradiation.
4. Such hormones as acetylcholine and adrenaline are mediators between the nervous system and tissues. It seems possible that microwave radiation may modify the activity of these mediators.

The question of whether there is general or selective reactivity of the endocrine system in an organism exposed to microwaves cannot be answered definitively. So for there have been no complex endocrinological investigations in animals or in men exposed to this kind of radiation. Among over 130 biological changes described following electromagnetic irradiation and listed in Report No. 2 from the Naval Medical Research Institute (9) some fourteen changes are of endocrinologic character.

In spite of the use of various classical and modern endocrinologic methods not all results obtained in different laboratories are in agreement. It seems that for studies of this kind on microwave irradiation control investigations and experimental procedure are of prime significance.

THE PITUITARY-THYROID AXIS

Convenient and sensitive tests for the functional evaluation of the pituitary-thyroid axis consist in the uptake of radioiodine by the thyroid gland under standard conditions and after its stimulation with thyroid-stimulating hormone (TSH).

The results obtained in groups of subjects professionally exposed to microwave radiation did not reveal any significant changes in radioiodine tests in comparison with similar tests in control groups (6, 7).

Recently Barański et al. (1) showed the stimulating influence of microwaves at 5 mW/cm^2 on the trapping and secretory functions of the thyroid gland in rabbits. These functional changes have been found to be in agreement with the histology of the thyroid tissue.

The simultaneously published results of Milroy and Michaelson (14) of their experiments on rats exposed to microwaves using power densities ranging from 100 mW/cm^2

in acute experiments to 10 mW/cm^2 or 1 mW/cm^2 in chronic experiments did not reveal any essential changes of the thyroid function.

It seems that it was the experimental procedure and conditions rather than the difference in animal species that might have been responsible for the discrepancies in the above-mentioned results.

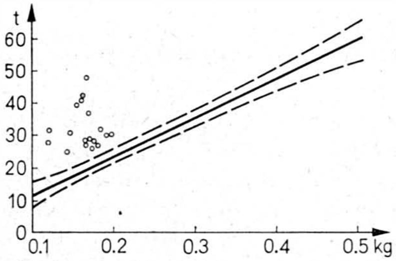

Fig. 1. The relation between body weight *m* in kg and survival time *t* in minutes. Continuous and interrupted lines denote the function *t* : *m* and 95% confidence limits, respectively, for 37 normal rats. The survival times of 18 hypophysectomized rats are denoted by circles which are non-linearly dispersed above the upper confidence limit of survival time for normal rats.

Conditions of irradiation: Frequency 2860—2880 MHz; far field in an anechoic chamber. Continuous plane wave with power density 120 mW/cm^2. The rats were irradiated individually in perforated cages made from polymethacrylate.

Table 1

Corticosterone determined fluorometrically in the adrenals and in blood plasma of male rats which had been accustomed for a fortnight to experimental procedures before their exposure to microwave radiation compared to rats that had not been so accustomed. Conditions of irradiation:

Frequency 2860—2880 MHz; far field in an anechoic chamber.

Continuous plane wave with power density 10 mW/cm^2. $\bar{X}$ ± S. D. — mean and standard devision.

Experimental procedure	Group of animals (in parentheses number of animals)	Corticosterone in	
		Adrenals μg/100 mg $\bar{X}$ ± S. D.	μg/100 mg $\bar{X}$ ± S. D.
Male rats unaccustomed to experimental procedures	Control (2)	14.2 — 15.4	28.8 — 29.0
	Irradiated during 15 minutes (2)	14.9 — 16.4	26.4 — 28.8
Male rats accustomed during a fortnight to experimental procedures before irradiation	Control (4)	5.6 ± 0.45	18.5 ± 3.3
	Irradiated during 15 minutes (4)	4.8 ± 1.10	22.2 ± 3.0
	Control (4)	4.5 ± 1.04	29.0 ± 2.3
	Irradiated during 30 minutes (4)	4.3 ± 1.70	

Indirect evidence has been obtained that the lowered general and tissue metabolic rate following hypophysectomy exerts some protective influence on the time-related lethal exposure of rats to microwave radiation. It was found that the survival period of normal rats exposed to microwaves was largely a function of body mass. Survival period per unit of body weight was significantly longer in hypophysectomized than in normal rats (Fig. 1).

THE PITUITARY-ADRENOCORTICAL AXIS

The functional relation between these two endocrine glands under normal conditions shows clearly a circadian rhythm. Numerous environmental factors potentiate the activity of this axis, inducing what is known as a stress reaction. It has been shown that excessive heat can be a powerful stress factor activating the pituitary-adrenocortical axis. Heat stress due to a high power density of microwaves may also be such an activating factor. However, moderate or low power densities of microwaves, being insufficient to produce a thermal effect, probably cannot elicit a stress reaction.

In short-term experimental procedures, especially in the investigation of the pituitary — adrenocortical axis, the need to adapt the animals to new environmental conditions before a proper experiment is obvious. The rats accustomed to experimental procedures did not show a stress reaction following short-term exposure to microwave irradiation (Tab. 1).

THE PITUITARY-GONADAL AXIS

The external localization of the male gonads, the high rate of cell divisions and differentiation, and the fact that the main route of heat dissipation is through the blood vessels of the scrotal skin are probably the principal factors responsible for the high sensitivity of these organs to microwave irradiation.

At various power densities of microwaves histologic and functional changes in the testes have been observed in experimental animals (4, 11) and in men (16, 17).

In the course of chronic microwave irradiation of different animal species both normal reproduction (5, 12, 15) and seriously disturbed reproduction have been described (2).

Gunn et al. (11) suggested that the androgenic hypofunction of interstitial gonadal tissue (Leydig cells) in rats exposed to microwaves could be of extragonadal origin, due to a diminished reactivity of these cells to LH or to reduced LH in the hypophysis.

From the results presented in Tables 2, 3 and 4 it is evident that there were no consistent pathologic changes in the amounts of gonadotropins (LH and FSH) after chronic or short-term exposure of rats to nonthermal doses of microwaves. However, single or repeated exposure of rats to such power densities induced detectable shifts of hypophyseal gonadotropic activities. In general, the content of LH and FSH in the hypophysis was augmented in animals killed immediately and was diminished in animals killed 18—20 h after irradiation.

In the hypophysis of animals exposed to lethal power density levels (2880 MHz, 150 mW/cm^2) the content of FSH, LH and GH was unchanged in comparison to that in control animals (unpublished data).

Table 2

The amounts of gonadotropins (LH and FSH) in the anterior pituitary gland of control male rats and of male rats exposed to microwaves 2 hours daily between April 23 and May 27, 1971. The pituitary gland has been excised at autopsy 18—20 hours after the last irradiation of animals. LH and FSH were assayed at one dose level by the ventral prostate augmentation test (Christiansen, 1968) and by the ovarian augmentation test (Evans et al., 1939) in hypophysectomized immature male and female rats, respectively. The standards, i. e. NIH-LH-S15 and NIH-FSH-S7, were assayed at three dose levels (these standards were obtained from the National Institute of Health, Endocrinology Study Section, Bethesda, USA). Conditions of irradiation:

Frequency 2860—2880 MHz; far field in an anechoic chamber. a) continuous wave with power density of 10 mW/cm^2; b) pulsed wave repetition rate of 800 Hz and average power density of 10 mW/cm^2.

$\bar{X}$ ± S. D. ± S. E. — mean and standard deviation or standard error.

Group of animals	Body weight in g $\bar{X}$ ± S. D.		μg/pituitary	
	initial	final	LH $\bar{X}$ ± S. E. (limits)	FSH $\bar{X}$ ± S. E. (limits)
I. Control rats 10 ♂♂ kept all the time in plastic cages in the animal house	39 ± 11	171 ± 11	480 ± 56^{+} (390 — 700)	800 ± 24^{+} (730 — 840)
II. Control rats 10 ♂♂ kept 2 h daily in wire cages in a sound-proof chamber	32 ± 5	177 ± 7	444 ± 20^{+} (390 — 510)	740 ± 55 (620 — 810)
III. Irradiated rats 10 ♂♂ exposed 2 h daily, 10 mW/cm^2, continuous wave	35 ± 5	181 ± 10	368 ± 11^{+} (340 — 390)	870 ± 114 (680 — 1200)
IV. Irradiated rats 10 ♂♂ exposed 2 h daily, 10 mW/cm^2, pulsed wave	39 ± 5	177 ± 14	298 ± 33^{+} (230 — 380)	700 ± 11^{+} (680 — 720)

Difference significant at $p = 0.05$

OTHER HORMONAL CHANGES

The quantity of growth hormone estimated at the same time as LH and FSH tests showed no clear changes. Some experiments revealed a stimulatory effect of microwave irradiation on the amounts of GH in the hypophysis of rats whereas others showed an inhibitory influence (unpublished data). GH was estimated by the method of Greenspan et al. (10).

Rats injected with acetylcholine survived longer, whereas those injected with adrenaline survived for a shorter time than control animals during acute microwave irradiation (2880 MHz, 150 mW/cm^2) (unpublished data). Such an irradiation of adrenaline in solution accelerated its transformation into chromogenic derivatives, e.g. adrenochrome. This process has been shown to be indistinguishable from that after conventional heating of adrenaline solutions (13).

Table 3

The amounts of gonadotropins (LH and FSH) in the anterior pituitary gland of control male rats and of male rats exposed once during 6 hours to microwave radiation. The pituitary gland was excised at autopsy made immediately after exposure of the animals. Conditions of irradiation, assays of gonadotropins and other indications the same as described in Table 2.

Group of animals	Body weight in g $\bar{X}$ ± S. D.	μg/pituitary	
		LH $\bar{X}$ ± S. E. (limits)	FSH $\bar{X}$ ± S. E. (limits)
I. Control rats 10 ♂♂ kept all the time in plastic cages in the animal house	270 ± 23	246 ± 20 (190 — 310)	493 ± 25 (430 — 540)
II. Control rats 10 ♂♂ kept from 7.00 a. m. to 1.00 p.m. in wire cages in a sound-proof chamber	244 ± 14	292 ± 27 (230 — 390)	510 ± 59 (370 — 660)
III. Irradiated rats 10 ♂♂ exposed, from 7.00 a. m. to 1.00 p. m., to 10 mW/cm², continuous wave	262 ± 18	428 ± 44 (300 — 500)	702 ± 53 (600 — 800)

Difference significant at $p = 0.05$ for FSH group I : III

Table 4

The amounts of gonadotropins (LH and FSH) in the anterior pituitary gland of control male rats and of male rats exposed to microwave radiation 2 hours daily from Dec. 14, 1972 to Jan. 10, 1973. The pituitary gland was excised at autopsy made immediately after the last irradiation of animals.

Conditions of irradiation, assays of gonadotropins and other indications are the same as described in Table 2.

Group of animals	Body weight in gm $\bar{X}$ ± S. D.	μg/pituitary	
		LH $\bar{X}$ ± S. E. (limits)	FSH $\bar{X}$ ± S. E. (limits)
I. Control rats 10 ♂♂ kept 2 h daily in double screened cage placed near the anechoic chamber	207 ± 21	408 ± 32 (310 — 470)	805 ± 55 (670 — 940)
II. Irradiated rats 10 ♂♂ exposed 2 h daily to 5 mW/cm², continuous wave	220 ± 22	520 ± 47 (400 — 630)	1306 ± 92 (1000 — 1720,

Difference significant at $p = 0.05$ for FSH group I : II

COMMENTS

The links between nervous and endocrine systems are multiregional in the body, but the main one is situated in the hypothalamus. Going down from the hypothalamic centers through the hypophysis to peripheral glands a stepwise amplification of hormonal stimuli may be observed. Thus the whole endocrine system displays some characteristics of a biological amplifier with the hypothalamus as the most sensitive and crucial region.

Unpublished preliminary results obtained with hypothalamic extracts from control and irradiated rats indicate that the time-related quantitative changes of hypophyseal gonadotropins described above can depend on the blocking or inhibitory effects of microwaves on the secretion of releasing hormones in hypothalamic centers. This assumption is consistent with the observed quantitative changes in neurosecretory granules in cells of hypothalamic centers of animals exposed to electromagnetic radiation (18, 19).

The harmful effects of microwave radiation on testicular and perhaps on other endocrine functions could be of both local and central (hypothalamic) origin.

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BIOLOGIC EFFECTS OF RADIATION IN THE 30—300 MHZ RANGE

T. V. Kalada, P. P. Fukalova and N. N. Gončarova

Institute of Industrial Hygiene and Occupational Diseases, Leningrad; Institute for Scientific Research on Industrial Hygiene and Occupational Diseases of the Academy of Medical Sciences of the USSR, Moscow, and Institute of Industrial Hygiene and Occupational Diseases, Harkov, USSR

This communication presents some general results of investigations conducted during many years on the biologic action of continuously generated electromagnetic fields of non-thermal intensity within the range of 40—200 MHz. The studies were directed at hygienic, clinico-physiologic and experimental aspects.

A complex clinical examination of a large number of specialists working with generators of ultra-high-frequency energy made it possible to define various health deviations in these workers (2, 3, 5, 14). The examination of this group of people aged under 40 years with a history of occupational exposure of over 5 years demonstrated the frequent occurrence of functional changes in the central nervous system (52%). No organic lesions were found. A vegetative dysfunction was the principal form of neurodynamic disturbances. The symptoms included hyperhidrosis, persistent red dermographism and enhancement of the pilomotor reflex, all of a mild degree. However, examination of the functional status of higher vegetative centers by means of special diencephalic tests disclosed quite frequently various anomalies of the thermoregulatory reflexes (distortion, inhibition, lack). Thermoasymmetry and isothermy were sharply expressed. Disturbances of photoreactivity of the skin took the predominant form of a lowered threshold sensitivity to ultraviolet radiation. The vegetative dysfunction was accompanied by neurasthenic (hypersthenic) symptoms in 14% of cases. In no case were well-developed forms of asthenia observed. The relationship between the frequency of neurodynamic disturbances and the length of work was clear-cut. The nervous pathology was somewhat more frequent in women (54%) than in men (48%). Circulatory pathology (hypertension, myocardiodystrophy, cardiosclerosis) was found in 24% of those examined. The histories of these patients did not reveal any factors which might have led to lesions of the heart muscle. A number of functional shifts of predominantly sympathicotonic nature were disclosed. Oscillographic data revealed raised hemodynamic parameters. Capillaroscopy visualized spastic and spastic-atonic pictures of the capillaries. Electrocardiographic examinations established a high frequency of moderate impairment of oxygenation of the heart muscle (in 42 out of 50 patients under 40 years of age, with negative histories). Cholesterol metabolism was investigated in the whole group and included measurements of total cholesterol, protein-bound cholesterol and total phospholipids. The level of loosely protein-bound cholesterol was elevated, and the ratio of phospholipids to cholesterol was lowered. In those working for over 5 years, also the total cholesterol content was elevated.

The combination of the two interdependent factors — neurocirculatory and metabolic disturbances which accompanied long exposures to electromagnetic fields of the meter range — played a significant role in the development of circulatory pathology.

Changes in the gastrointestinal tract were found in 14% of cases (chronic gastritis, 12%; ulcers, 2%). In half of the cases, gastritis was diagnosed in young patients. It should be noted that in all patients gastric lesions developed against a background of neurasthenia syndrome and vegetative dysfunction. No quantitative changes in the peripheral blood were found. Some deviations in the physicochemical and functional properties of the erythrocytes and leukocytes were observed. A lowered osmotic resistance of the leukocytes of those examined occurred six times more frequently than in controls. The phagocytic reaction was also lowered and led to a weakened immunobiological reactivity of the organism. The increase in functional disturbances with longer periods of work in electromagnetic fields, taken together with sharp differences in health status between those working with sources of electromagnetic fields and their controls, point to a link between the changes and the occupational factors.

Analysis of data of experimental investigations conducted both in factories (7, 13) and under laboratory conditions on workers and volunteers (8, 9, 10, 11, 12) showed that electromagnetic fields of non-thermogenic intensity are indeed harmful and may produce cumulative effects.

Accumulation of biological effects is reflected in resetting of functional systems of the organism to a new level of activities.

In this way statistically significant phasic changes in the initial level of the functional status of the thermic skin analyser, and of circulatory and central nervous systems in those working for various lengths of time were ascertained. Figure 1 may serve as an illustration.

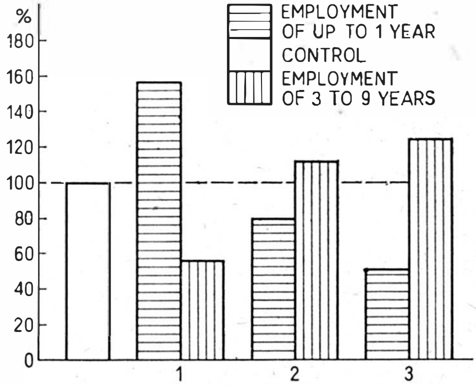

Fig. 1. Changes in the level of activity of thermal receptors (1), threshold temperature sensitivity (2) and threshold excitability of the visual analyser (3) in workers with various duration of employment, as compared with the control group taken as 100%.

Figure 1 shows that electromagnetic fields had an activiting influence on those working for less than 1 year as manifested by changes in the pattern of thermal receptors as compared with the control group. With increasing length of work under conditions including irradiation with electromagnetic waves, the level of active thermal receptors sharply declined. The adjustment of thermal perception changed correspondingly. In those with a shorter length of work the threshold of heat perception was much lower than in controls, and in those working longer it was higher.

Phasic changes in the initial level of functional activity were recorded on investigating other analytical systems. Shortening of the latent period of reflexes to sound and light stimuli and a lowered value of the optical chronaxy in early periods of work were disclosed. These parameters lengthened with increasing length of work. Hemodynamic parameters reflected hypo- and hypertensive fluctuations during the working day and an increase of hypertensive states with lengthening occupational exposure.

On comparing results of physiologic investigations with physico-hygienic parameters of irradiation of workers, a clearcut relationship was noted between the character and level of reactions and intensity of the factor acting in the industrial environment.

Experimental data obtained in volunteers under laboratory conditions of irradiation mimicking industrial variants revealed certain principles concerning general physiologic responses of the human body towards electromagnetic fields. The thermoregulatory system, some systems of hemodynamics and thermal, optical and auditory analysers proved most functionally reactive and sensitive to the influence of experimental irradiation. The dynamics of functional deviations were compared with those accompanying the presumed action of the factor. The irradiation was systematic with daily 15 min exposures and the 30 days' duration of each series of treatments. The ambient temperature ranged from 22.6 to 23.4°C with relative humidity of 40—46%.

The results showed that some functional deviations took place during irradiation, while others followed it. The skin temperature of distal parts of the body (hands, feet) was elevated during the whole period of actual irradiation with simultaneous intensification of heat loss through emission and demobilization of heat receptors. The number of active cold receptors sharply increased.

Figure 2 presents the levels of the hand skin temperature, heat emission, and changes in the pattern of heat and cold receptors during simulated and actual irradiation.

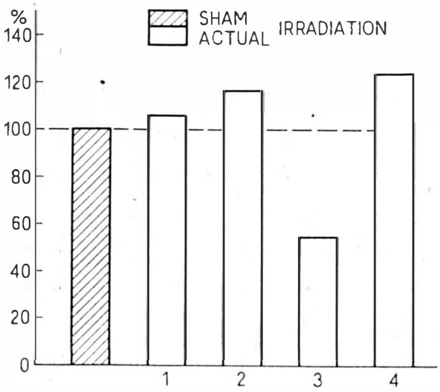

Fig. 2. The levels of indices of the hand skin temperature (1), heat emission (2) and changes in numbers of heat (3) and cold (4) receptors during actual and sham irradiation, the latter taken as 100%.

For assessment of the status of the temperature analyser, duration of the latent periods of the reflex to contact and radiated heat were measured. The visual and auditory analysers were also assessed. It was found that after irradiation, as well as during the whole period of the actual action of the stimulus, the duration of the reflexes was shortened. Thus the excitability of the analysers was increased. The initial values of hemodynamic parameters and of the pulse rate had a tendency to increase, apparently due to the irritation of the sympathetic nervous system by the field.

Results of investigations of regional blood circulation showed active vasomotor reactions not only during irradiation but also following it. Figure 3 illustrates fluctu-

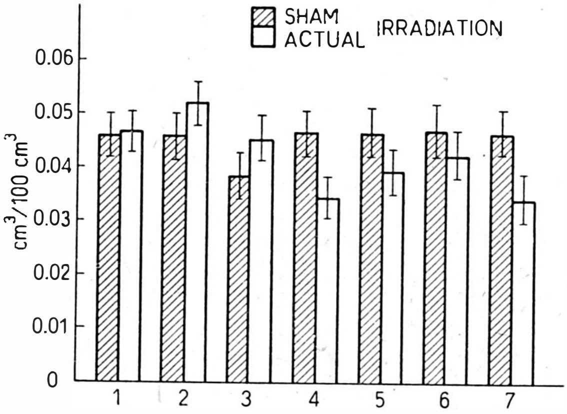

Fig. 3. Fluctuations in pulse volume during sham and actual irradiations. Symbols: 1 — initial readings, 2 — switching on of the generator, 3 and 4 — 15 and 30 min of irradiation, 5 — switching off of the generator, 6 and 7 — 15 and 30 min of recovery.

ations in pulse volume as recorded plethysmographically during simulated and actual irradiation. Switching on of the generator, as well as cessation of irradiation, were accompanied by an increase in pulse volume. Towards the end of irradiation and during the 30 min recovery period this value was lowered. In the conditions of the experiments the tonus of peripheral blood vessels was increased during the entire irradiation period with partial normalization following irradiation.

An analysis of the data showed that the initial increase in tonus resulted from an increase in pulse pressure, while in the process of irradiation it was due to spastic status of the peripheral vessels.

From the point of view of contemporary physiology, such shifts in physiologic systems from one functional level to another are regarded in some cases as adaptive responses to the action of exogenous irritants, and in others as exhaustion or functional weakening.

The experimental results obtained showed that the level of activity of the functions under investigation was changed; these changes may be regarded as adaptive responses.

However, repeated radiowave irradiation over a long period of time led to more serious functional disturbances, as evident from clinical symptoms. It follows that adaptive responses taking place during the initial stages of irradiation should be regarded in some instances as transient states with a potential for becoming pathologic.

The influence of electromagnetic fields upon the organism of animals was investigated in both acute and chronic experiments (5—8 months' irradiation), using thermal and non-thermal intensities, respectively (1, 4, 6, 15, 16, 17). The functional status of the central nervous system (electroencephalography, conditioned reflex activity, the threshold of neuromuscular stimulation, and others), hemodynamics, biochemical processes in the animal nervous tissue directly connected with its function (acetylcholine metabolism, some aspects of carbohydrate and nitrogen metabolism), protein metabolism and immunobiologic reactivity were all assessed. The morphology of various organs and tissues was studied.

The results of these investigations showed a definite dependence of biologic effects in the functional systems under study on the length of action of the irradiation and physical parameters of the latter (intensity, frequency and components of the field). The effects of thermogenic intensities were connected with evident disturbances of the nervous regulation and functional impairment of the hypophysis and suprarenal cortex. Functional disturbances of the nervous system were clearly connected with the exhausting influence of the causative factor (EM field) upon nervous cells with progressive inhibition, in some cases extremely severe. Sequelae of irradiation with nonthermogenic intensities were of the same character, though milder.

Investigations aimed at elucidation of animal brain metabolism were conducted to gain insight into some aspects of the mechanism of functional disturbances of the nervous system. The results of exposure to electric fields showed that glycogen hydrolysis was more intense and that oxidation of its intermediates was impaired (low glycogen and high lactic and pyruvic acid content). Chronic irradiation with magnetic fields led to glycogen accumulation in the tissues without changes in concentration of the other compounds under study. The findings were regarded as a result of lowered activity of the processes of glycogen utilization by the nervous tissue due to functional inhibition, as was established by physiologic investigations. The processes of carbohydrate metabolism in the brain were still abnormal one month after electromagnetic field action, indicating the long-lasting nature of the changes and, perhaps, the cumulative nature of bioeffects. Deviations of ammonia formation in the brain tissue were found to be a similar in character.

The functional status of the nervous system depends to a certain extent upon the acetylcholine level in the brain tissue. It was shown experimentally that, as a result of prolonged action with electromagnetic fields, the level of acetylcholine increased conspicuously and cholinesterase activity decreased. The former was evidently connected with disturbed processes of acetylcholine synthesis and binding to brain proteins. A lowered cholinesterase activity was of a compensatory-adaptive character.

Changes in immunobiologic reactivity had a phasic character, with periods of suppression of phagocytic and bactericidal blood functions alternating with increased activity.

Morphologic investigations showed hemodynamic disturbances and mild dystrophic changes in the parenchymatous organs (particularly in the liver), heart muscle and nervous system. In the central nervous system, changes in the ganglionic cells of the cortex and of subcortical nuclei were found; in the skin receptors there was partial fragmentation of nervous fibers with clearly visible swelling.

Thus the complex clinico-physiologic and experimental studies on the biologic action of electromagnetic fields made it possible to establish some general biologic trends in reactions of the human and animal organism, to elucidate some aspects of pathogenesis of functional deviations, and to prove their cumulative character.

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THE CHARACTERISTICS OF BIOLOGIC EFFECTS OF MICROWAVES COMBINED WITH THE ACTION OF SOFT X-RAY IRRADIATION AND HEAT

K.V. Nikonova and I.P. Sokolova

Labor Order of the Red Banner Institute for Scientific Research Industrial Hygiene and Occupational Diseases Academy of Medical Sciences of the USSR, Moscow, USSR

Under natural conditions, microwave irradiation is often accompanied by other factors in the industrial environment, such as X-ray irradiation, unfavourable weather conditions, noise and toxic compounds.

Studies on the character of the biological effects resulting from such combined influences are important for the solution of a number of hygienic questions, and for elucidation of the role played by the accompanying factors in the etiology of pathological processes occurring in those working with SHF generators.

The first publications on the combined action of microwaves and ionizing radiation appeared in the early sixties (4, 9, 14, 13, 17).

Experimental studies by American authors (13, 14, 17) provided interesting data on changes in sensitivity of the organism to microwave and gamma-irradiation, depending on the sequence of action of these factors.

The present communication presents the results of experimental studies on the combined action of microwaves and low energy (soft) X-ray irradiation, since earlier investigations (7, 15) showed that electronic equipment with an effective voltage of at least 10 kV, used in SHF installations, could be a source of X-rays.

Biological effects of the combined action of 10 cm microwaves and X-ray irradiation with $E_{ef} = 13 \times 5$ keV were studied.

In our work an RUM-7 (RUT 60—20—I) instrument was the source of X-rays with an anode voltage of 30 kV and 0.3 mm Al + 0.5 mm organic glass (the bottom of a cage) filtration. The dose rate was regulated by means of changes in current, and dosimetry was carried out with a KD-IM condensor dosimeter. Irradiation of animals was performed essentially from the abdominal side.

A 10 cm wavelength pulsed microwave generator was used. The power density of irradiation was controlled with a PO-I apparatus.

Investigations carried out at various power densities of SHF currents and different doses of soft X-ray irradiation made it possible to establish a relationship between the character of biological effects and intensity of action.

It was found that the combined action of high intensities of microwaves and of soft X-rays was synergistic (by synergism we mean the effect close to, or somewhat exceeding, summation). At the same time in the clinical picture lesions caused by X-rays were predominant. Thus, upon combined action of a single dose of 2500 r of X-rays and 15 min daily irradiations with 40 mW/cm² microwaves for 6 weeks, the clinical picture of the affected mice was that of developing radiation sickness, as manifest by changes in body weight, low leukocyte count in the peripheral blood, progressive skin lesions, and decreased weight of the testes.

The histological examination of the testicles revealed severe morphological changes testifying to atrophy and dystrophy of the seminiferous epithelium. According to a number of parameters, the lesions following the combined action were more severe than those resulting from X-rays or microwaves applied singly. Thus, with the combined action, the death rate of animals was higher, the loss of body weight was more marked, the skin lesions occurred earlier and were more evident, and the decline in number of leukocytes in the peripheral blood was more pronounced (Tab. 1, Fig. 1). This enabled the conclusion to be drawn that the action of high intensities of microwaves coupled with that of soft X-ray irradiation was synergistic.

Table 1

Reaction of white blood cells and mortality during the experimental period (2500 r, 40 mW/cm²)

Type of action	Leukocyte number		Died during 6 weeks (%)
	Background	3rd day	
Microwaves	10886 ± 412	8071 ± 588	5.0 ± 4.0
X-rays	10844 ± 410	7350 ± 514	5.5 ± 5.3
Combined	11814 ± 521	5300 ± 226	36.4 ± 10.2
Control	11190 ± 443	12514 ± 994	0 ± 4.5

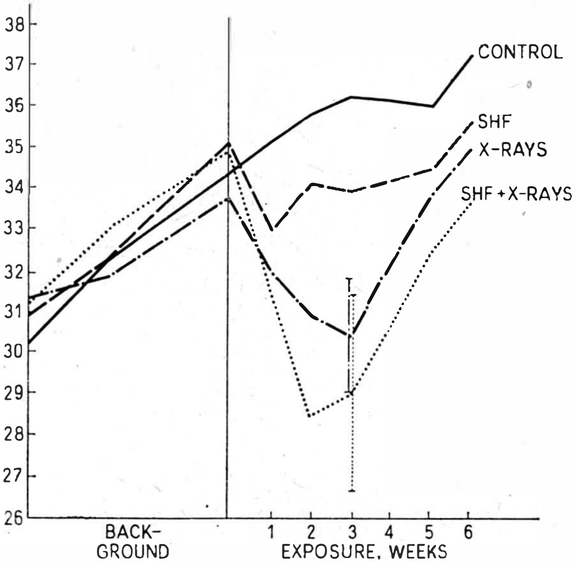

Fig. 1. Changes in body weight of white mice (2500 r, 40 mW/cm²).

However, of the greatest practical interest were the characteristics of those biological effects which resulted from low intensities of action, close to those of actual industrial conditions.

It should be noted that with the change to low intensities, the role of microwaves became more conspicuous and the manifestation and reproducibility of the "amplification" effect declined.

The following are results of studies on biological effects accompanying the combined action of 1 mW/cm² for 1 h daily and 25 r weekly. Under conditions of repeated, long-lasting, chronic experiments, investigations were made of the changes in body weight of the animals, the peripheral blood, permeability of the blood vessels, immunobiolo-

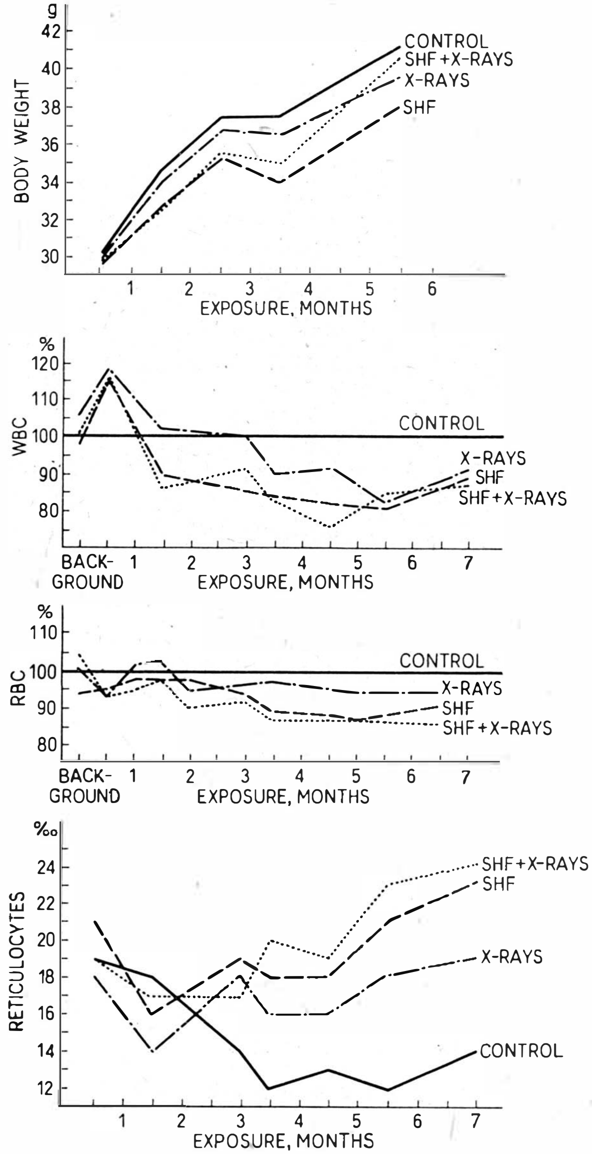

Fig. 2. Changes in body weight of white mice and in peripheral blood parameters of white rats (1 mW/cm², 25 r per week).

gical reactivity, functional status of the central nervous system (the labyrinth and EEG methods), weight of the testicles, reproductive function of males, as well as histological pictures of the organs and tissues of the irradiated animals.

Analysis of the collected data showed that the combined action of microwaves and soft X-ray irradiation at the level of low intensities was governed by biological laws which differed from those prevailing at high intensities.

Under conditions of the combined action of low intensities no well-defined intensification of biological effects was observed. According to a number of parameters the observed extent of the changes was close to that characteristic of the factors applied singly.

The pattern of the reactions in different organs and systems was defined in some cases by the action of radiowaves, and in others by X-rays.

According to weight changes and the peripheral blood picture the groups of animals acted upon with the combined agents behaved in a way analogous to those subjected to microwave irradiation alone (Fig. 2).

Following the combined action, in a number of experiments during separate periods of observation the animals lagged behind in weight gain. We could observe an analogous effect also with isolated radiofrequency irradiation, and in none of the experiments were significant differences noted in this parameter between the groups.

In the peripheral blood of animals changes were found following the combined action of microwaves and soft X-rays and took the form of lowered leukocyte and erythrocyte counts and increased reticulocyte numbers, very much like those accompanying isolated microwave irradiation. Some differences noted between these groups in individual cases were, as a rule, transient and poorly reproducible in repeated experiments.

Related to the action of microwaves was a marked hyperplasia of reticuloendothelial elements in the liver and spleen, of lymphoid elements in the lungs, and of microglia in the brain, as well as manifestations of irritation of the receptor apparatus of the skin and a decrease in ribonucleoproteins of the epidermis and its derivatives.

The second factor of the combination, X-ray irradiation, determined the lowered weight of the testicles, increased vascular permeability and, as consequences of the latter detectable upon histological examination, an increased content of mast cells and plasmocytes in the subcutaneous tissue, of mast cells in the connective tissue surrounding the spleen, and of iron-containing pigment in the pulmonary lymph nodes and spleen (Tab. 2, Fig. 3).

Finally, the reactions of a number of organs and systems under conditions of combined action were determined by both microwave and X-ray irradiation.

Table 2

Weight of testicles in percentages of body weight of mice (1 mW/cm^2, 25 r per week)

Type of radiation	Duration of action	
	4 months	11 months
Microwaves	0.61 ± 0.03	0.53 ± 0.02
X-rays	0.47 ± 0.03	0.46 ± 0.015
Combined	0.51 ± 0.02	0.45 ± 0.02
Control	0.61 ± 0.02	0.58 ± 0.034

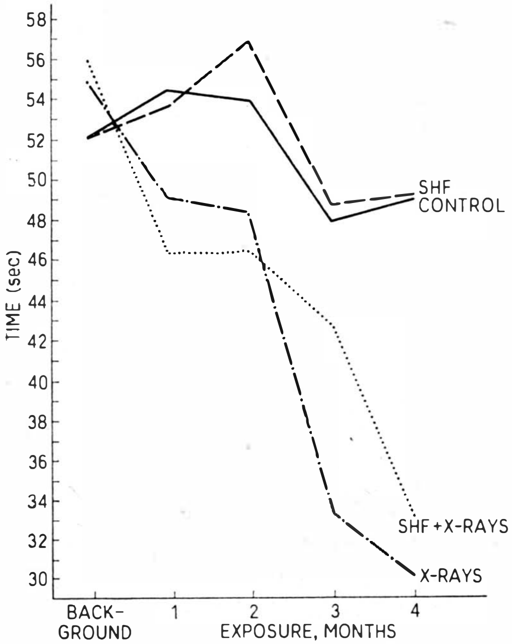

Fig. 3. The state of vascular permeability (1 mW/cm², 25 r per week).

Thus, during studies of immunobiological reactivity over a period of 6 months, various changes in the phagocytic and digestive functions of neutrophils, and also in the bactericidal power of plasma, were observed. During different periods of the study, the consequences of one or the other factor predominated. As to their intensity, the

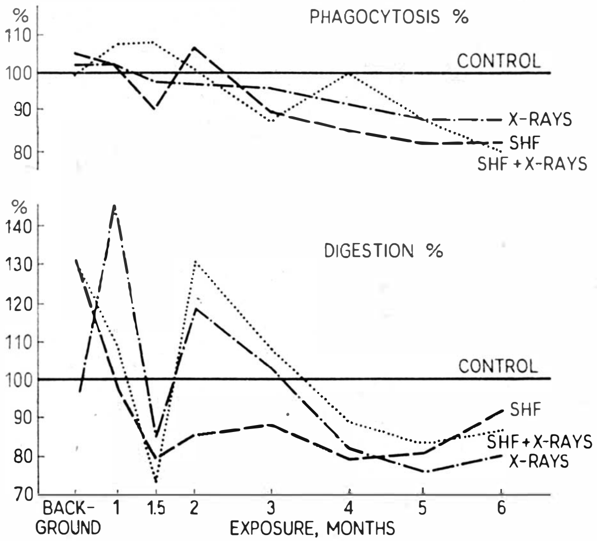

Fig. 4. Changes in indicators of immunobiological reactivity (1 mW/cm², 25 r per week).

changes due to the combined action were indistinguishable from those observed following exposure to the separate factors (Fig. 4). In the testes, following long periods of action, marked dystrophic changes in the seminiferous epithelium were detected as elicited predominantly by X-rays. They were accompanied by homogenization and interstitial edema beneath the capsule and proliferation of the interstitial elements due to microwave irradiation. The process was focal in character which might apparently explain the lack of more pronounced changes in reproductive capacity of the animals by comparison with the influence of a single factor.

Thus, the biological effects of the combined action of low-intensity microwaves and soft X-ray irradiation were characteristic of both the former and the latter factor. No clear-cut intensification of the biological effects by comparison with those induced by the separate factors was observed.

Other investigators (5) came to analogous conclusions while studying the combined action of microwaves of 12.6 cm wavelength and X-ray irradiation of E_{ef} of 73 and 10 keV.

It is true that some authors have reported that functional changes of the central nervous and circulatory systems were somewhat more pronounced in people working under conditions of the combined action of SHF and X-ray irradiation than in workers subjected mainly to the action of microwaves. At the same time these authors noted that the changes did not exceed the range of physiological fluctuations.

Another combination of factors — microwaves and heat — is equally interesting from both the theoretical and practical points of view.

There are data in the literature about more pronounced changes in the health status of people subjected to microwave irradiation under conditions of tropical climate (6, 10). American investigators (12) observed that, following the combined action of microwaves and heat, weight loss and susceptibility to microwave irradiation in dogs were more pronounced. Some authors (16) deem it necessary to differentiate the safe exposure levels taking into account a temperature factor.

We studied the biologic effects of the combined action of 10 cm microwaves and high air temperature. To create the temperature conditions needed, use was made of a chamber with hot air supplied by a heater.

As in the case of combination with ionizing radiation, biologic effects were found to depend on levels of exposure.

Table 3

Survival of animals in SHF fields as a function of ambient temperature

Type of animal	SHF power density (mW/cm²)	Air temperature (°C)	Mean survival time (min)
Mice	80	40	28.3 ± 1.8
	80	22	63.3 ± 7.6
	80	14	106.5 ± 4.5
Rats	60	40	43.3 ± 3.2
	60	20	111.5 ± 4.7

Investigations of the survival rate of white mice and rats showed that the higher the ambient temperature the more rapid was the death of the animals in SHF fields (Tab. 3).

Thus, with a reduction in temperature from 40°C to 14°C, the duration of life of white mice irradiated at a power density of 80 mW/cm² increased from 28.3 ± 1.8 to 106.5 ± 4.5. An analogous result was obtained in rats. A similar observation has been recorded in the literature (11).

An analysis of the thermal reactions of white rats with changes in irradiation conditions showed that, under conditions of impaired heat emission due to failure of compensatory mechanisms, the body temperature increased faster under the combined action and caused an earlier death of the animals.

The synergism of action of microwaves and heat was clearly evidenced at the intensity level of 10—15 mW/cm² and 38—40°C. Experiments performed on mice showed that a single exposure to the combined action at these intensities led to a more pronounced loss of physical endurance than following exposure to microwaves or temperature alone. During chronic experiments, the highest number of reinforcements for attaining the criterion of strengthening the previously elaborated conditioned defence reflexes of "escaping" was required following exposure to both factors.

In rats under chronic exposure conditions a stronger biological effect was noted with the combined action according to such indicators as weight changes and vascular tonus.

Studies of the bioelectric activity of rabbit brain showed that EEG effects following the combined action o SHF and heat were of the same character as those caused by SHF or heat alone, but exceeded the latter in severity.

We now move on to the combined action of heat and lower intensities of microwaves. Results of investigations on the combined action of microwaves and heat of 5 mW/cm² and 40°C intensities, respectively, under conditions of chronic exposure have been reported (2).

The author found that previous microwave irradiation increased the sensitivity of white rats to thermal exposure as evidenced by a greater rise in rectal temperature, a tendency towards increased numbers of erythrocytes, lowered viscosity of the blood, decreased percentage of pregnant rats and average size of the litter, and lowered weight coefficients of the liver and spleen.

In rats exposed daily for 1 h simultaneously to the combined action of microwaves and heat at intensity levels of 1 mW/cm² and 35—38°C we investigated the following indicators: thermal reaction, weight changes, immunobiological reactivity, blood pressure and cholinesterase activity of blood erythrocytes.

Analysis of the results showed that the combined action at low intensities was characterized by the absence of clear-cut intensification of biologic effects by comparison with exposure to microwaves or heat alone, and the presence of symptoms characteristic of either of the factors.

An increase in body temperature of white rats following the combined exposure did not exceed that resulting from heat exposure alone. At the same time, return to the initial temperature after cooling at 4—6°C for 1 h was faster than in animals submitted to microwave irradiation alone, while the prolonged influence of heat resulted in some slowing of the process of recovery.

Investigations of immunobiological functions (phagocytic and digestive activity of neutrophils, bactericidal properties of plasma, the course of inflammatory processes) lasted for 6 months and showed that at various times and according to different indicators the changes following the combined action were either of a "microwave" type or analogous to the "thermal" type. At the same time no significant differences from data on the isolated action of each of the factors were detected.

An interesting result was obtained upon investigating the blood pressure. Simultaneous combined exposure elicited increased arterial pressure analogous to that observed with thermal exposure alone. However, functional loading in the form of intraperitoneal injection of 0.1% adrenalin solution (1 mg per kg body weight) enabled detection of a more pronounced increase in vascular tonus in the case of combined exposures (Fig. 5). Thus, according to increase in blood pressure 45 and 60 min after injection, the latter group differed significantly from the "thermal" one ($p < 0.05$).

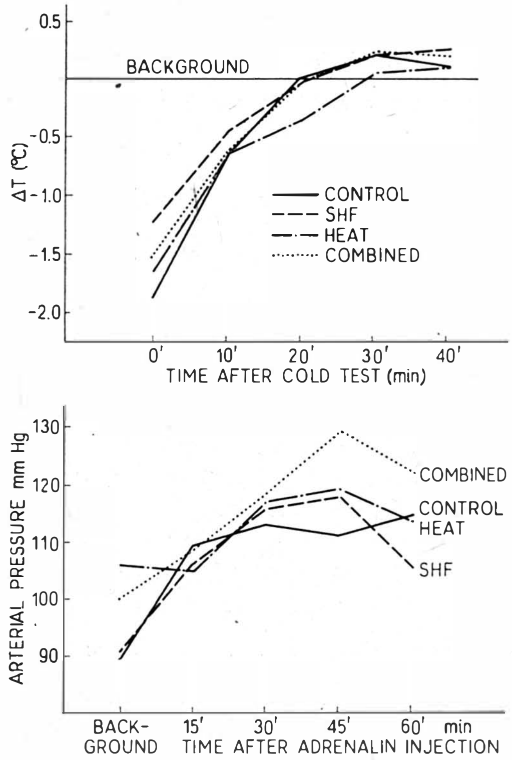

Fig. 5. Results of functional tests (1 mW/cm², 38°C): a) restoration of body temperature after cold test, b) changes in arterial pressure upon adrenalin injection.

More pronounced changes in vascular tonus following combined action of microwaves and heat were validated by data (8) on breakdown of adaptation to infrared rays and elevated ambient temperature under the influence of microwaves (wavelength, 12.6 cm; power density, 1 mW/cm²): thermal exposure following microwave irradiation resulted in changes of arterial pressure irrespective of the number for such tests.

The presence of such effects points to the necessity for further accumulation of experimental materials. Particular attention should be paid to those systems providing for regulatory and adaptive functions of the organism (central nervous, cardiovascular and endocrine-humoral systems).

Dependence of the character and severity of biologic effects upon the intensity and sequence of action of factors has been described in the literature for combinations of microwaves with reduced air pressure (8), and also for joint action of other physical and chemical factors (1, 3). This suggests that in order to elucidate the character of the combined action of factors one should not limit oneself to a single level of action. Intensities employed in experiments should be determined by practical problems, the solution of which was the aim of the present study.

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INFLUENCE OF MICROWAVE RADIATION ON THE HEMATOPOIETIC SYSTEM

P. Czerski, E. Paprocka-Słonka, M. Siekierzyński and A. Stolarska

Department of Human Genetics, National Research Institute of Mother and Child, Warsaw; Military Institute of Aviation Medicine, Warsaw, and Institute for Postgraduate Study of the Military Medical Academy, Warsaw, Poland

A review of the literature (see 3, 8, 12 for bibliographies) demonstrates that acute microwave exposure may induce transient changes in the peripheral blood picture dependent on exposure conditions (field intensity, duration etc.) and animal species. Such effects may be explained by displacement of blood cells between the blood stream and tissues, as well as by displacement of body water. Divergent reports on the effects of repeated exposure exist. In the case of long-term, low-dose exposure most authors stress a tendency to a slight decrease in RBC counts and a peripheral lymphocytosis (1, 2, 3, 5, 6). Nevertheless negative reports stressing the lack of effects of exposure exist (5, 12, 14).

Only a few reports concerning microwave effects on the hematopoietic tissue itself and hematopoietic function exist. Those of Michaelson (10, 11), Barański (1, 2), Miro (this volume) and Yagi (this volume) should be mentioned. Barański found that long-term, low-dose exposure induces stimulation of lymphopoiesis in the bone marrow, lymph nodes and spleen of rabbits and guinea pigs. Moreover this author described nuclear structure anomalies and aberrations of mitosis in the lymphocytic and erythroblastic cell lines of long-term irradiated animals. Michaelson described disturbances in iron metabolism of repeatedly exposed dogs and shortening of red cell life time.

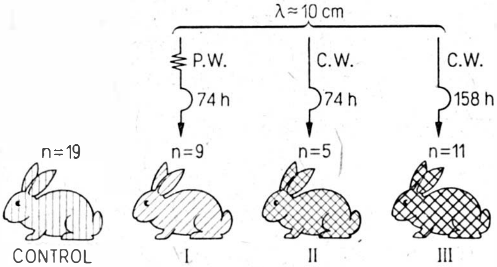

Fig. 1. The experimental system used in the first series of experiments: animal groups and irradiation conditions.

In view of this it seemed interesting to investigate microwave effects in the lymphocytic and red cell systems. The aim of this work is to present briefly the principal findings of several series of experiments designed to examine such effects.

In the first series of experiments 3 groups of rabbits were exposed in an anechoic chamber to 2950 MHz pulsed (1200 MHz, 1 μs) or CW microwaves at 3 mW/cm^2 2 h daily for a total of 74 or 158 h, a 4th group of animals serving as controls (Fig. 1). The irradiated animals were restrained in plastic cages and placed with head directed to the source (horn-antenna) in the far field zone. Control temperature measurements at various points of the body in yet another group of animals did not demonstrate a temperature rise over 0.5°C after irradiation. At the end of the irradiation period 1.5 μCi/kg body weight of ^{59}Fe citrate was introduced into the marginal vein of the ear and 100 minutes later the first blood sample was withdrawn for hematologic and radioactivity determination (Fig. 2). Using routine methods ferrokinetic indices were calculated. The results obtained are described in more detail elsewhere (5, 13), but the principal findings are illustrated on Figures 3—7. Significant differences between the control group and the experimental groups were demonstrated.

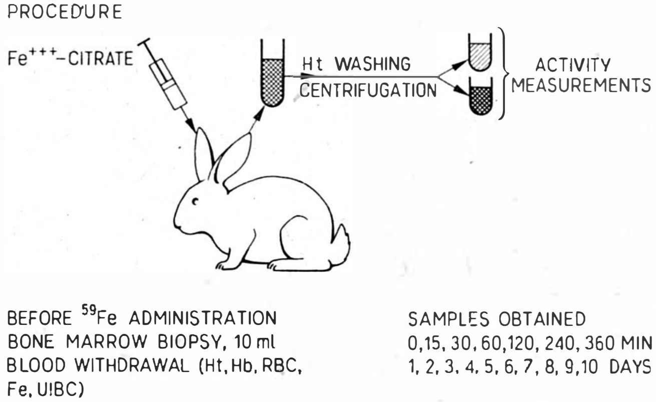
PROCEDURE
Fe^{+++}-CITRATE
Ht WASHING
CENTRIFUGATION
ACTIVITY MEASUREMENTS
BEFORE ^{59}Fe ADMINISTRATION
BONE MARROW BIOPSY, 10 ml
BLOOD WITHDRAWAL (Ht, Hb, RBC, Fe, UIBC)
SAMPLES OBTAINED
0, 15, 30, 60, 120, 240, 360 MIN
1, 2, 3, 4, 5, 6, 7, 8, 9, 10 DAYS

Fig. 3. Radioactivity half-time.

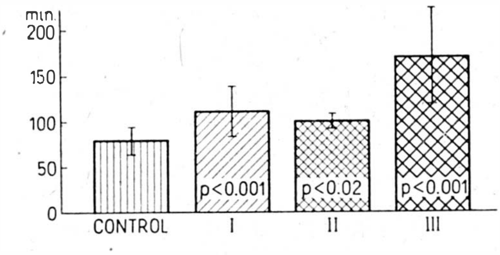

Fig. 3. Radioactivity half-time.

Perhaps the most interesting finding is that 74 h of exposure to pulsed microwaves (group I) induced much more pronounced effects than exposure to CW (group II) of the same duration, the differences between both these groups being highly significant. On the other hand 158 h exposure to CW microwaves (group III) induced very similar effects to those of exposure to pulsed microwaves of half that duration.

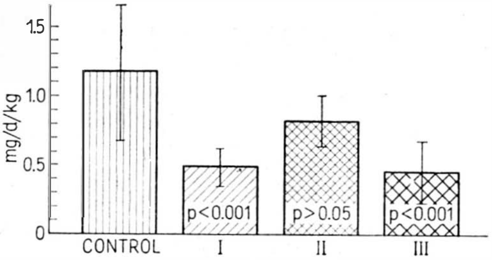

Fig. 4. Iron transport rate.

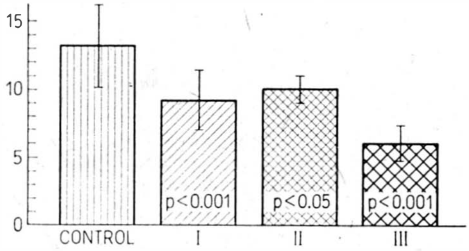

Fig. 5. Iron turnover rate.

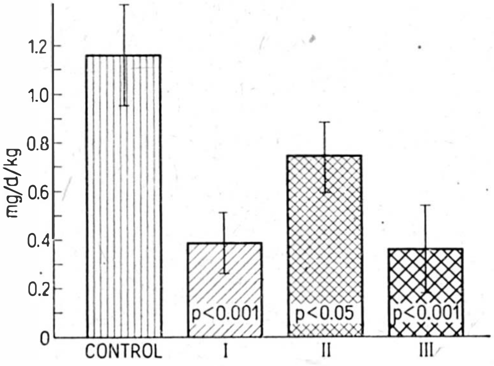

Fig. 6. Quantity of iron incorporated into erythrocytes.

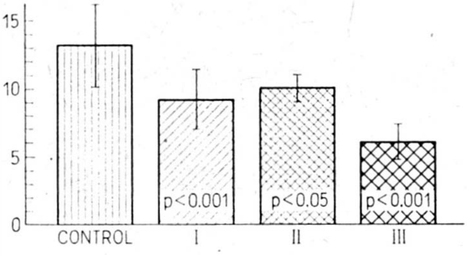

Fig. 7. Percent erythrocyte production.

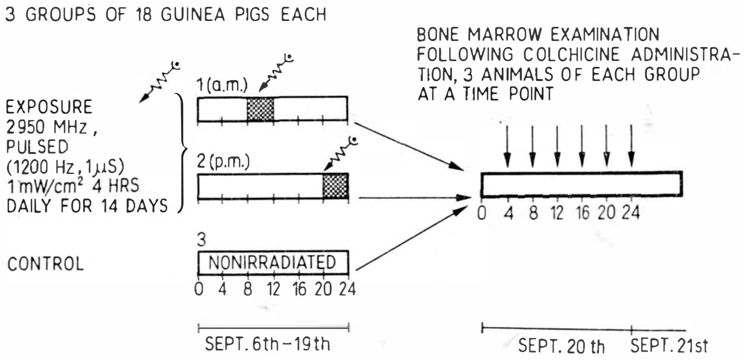
3 GROUPS OF 18 GUINEA PIGS EACH
EXPOSURE
2950 MHz,
PULSED
(1200 Hz, 1µS)
1 mW/cm² 4 HRS
DAILY FOR 14 DAYS
1 (a.m.)
2 (p.m.)
3
CONTROL
NONIRRADIATED
0 4 8 12 16 20 24
BONE MARROW EXAMINATION
FOLLOWING COLCHICINE ADMINISTRATION, 3 ANIMALS OF EACH GROUP
AT A TIME POINT
0 4 8 12 16 20 24
SEPT. 6th-19th
SEPT. 20 th
SEPT. 21st

Fig. 8. Experimental system used in the second series of experiments (guinea pigs).

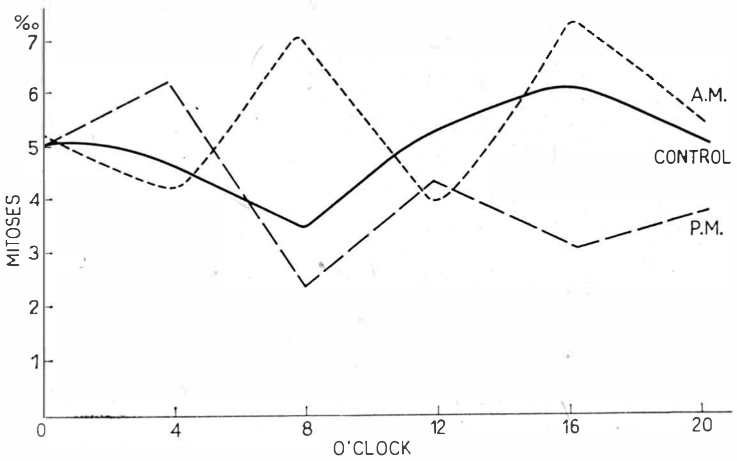

Fig. 9. Rhythm of mitoses in bone marrow cells (stem cells) of control and a. m. or p. m. irradiated guinea pigs.

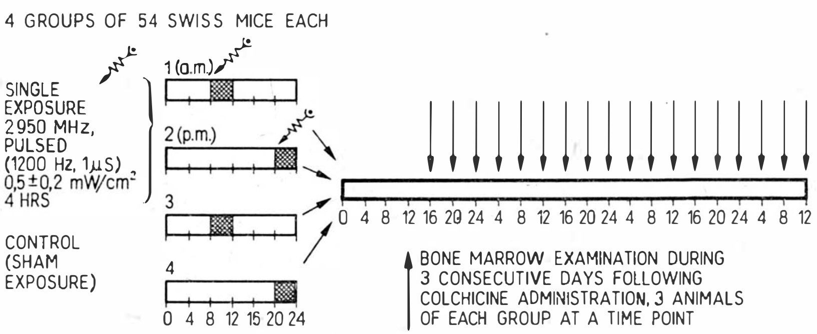
4 GROUPS OF 54 SWISS MICE EACH
SINGLE
EXPOSURE
2950 MHz,
PULSED
(1200 Hz, 1µS)
0,5±0,2 mW/cm²
4 HRS
1 (a.m.)
2 (p.m.)
3
4
CONTROL
(SHAM
EXPOSURE)
0 4 8 12 16 20 24
0 4 8 12 16 20 24 4 8 12 16 20 24 4 8 12 16 20 24 4 8 12
BONE MARROW EXAMINATION DURING
3 CONSECUTIVE DAYS FOLLOWING
COLCHICINE ADMINISTRATION, 3 ANIMALS
OF EACH GROUP AT A TIME POINT

Fig. 10. Experimental system used in the second series of experiments (mice).

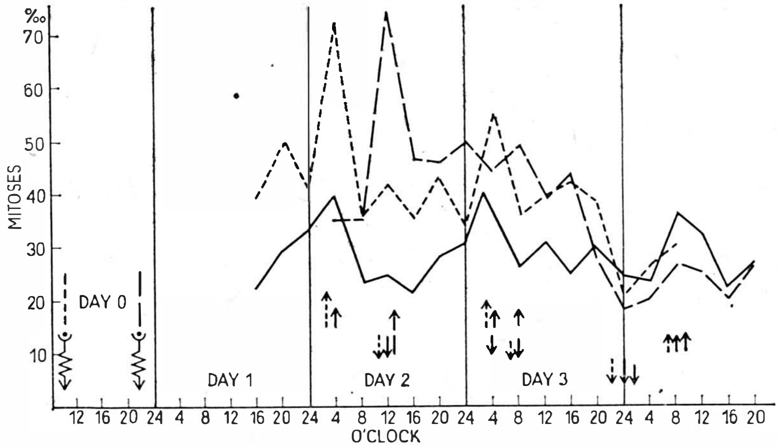

Fig. 11. Total mitotic index of bone marrow cells in control and a. m. or p. m. irradiated mice.

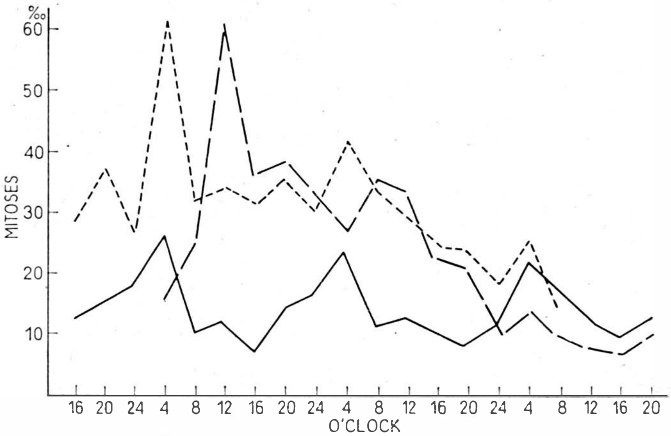

Fig. 12. The mitotic index of stem cells (undifferentiated and lymphocyte-like cells) in the bone marrow of control and a. m. or p. m. irradiated mice.

The second series of experiments concerned effects of microwave exposure at various times of the day on the circadian rhythm of bone marrow cell mitoses. Once more the full details are described elsewhere (4, 7). In one of these experiments repeatedly exposed guinea pigs were used (4). The experimental system is presented in Figure 8. No marked differences between control animals and irradiated ones were seen in the circadian rhythm of recognizable precursors of granulocytes and erythroblasts. In the cell category classed as bone marrow stem cells (early erythroblasts, myeloblasts, hemopoietic stem cells and probably lymphocytes) a distinct change both in amplitude and phase of the circadian rhythm of cellular divisions was noted in animals irradiated in the evening or in the morning, as compared with one another and with the control group (Fig. 9). The statistical significance of these findings may be questioned, because of both the short observation period and the small number of animals. In view of this syngeneic mice were subjected to a single exposure (a.m. or p.m.) and examined during 3 consecutive days beginning 28 h after the termination of irradiation (Fig. 10). It was reasoned that if in reality microwave exposure induced changes in the circadian rhythm of bone marrow cell mitoses, a disturbance resembling a decaying oscillation should be obtained. The results confirmed the expectation (Fig. 11), a disturbance in the amplitude and phase of the mitotic rhythm of cells belonging to the "stem cell" category being responsible for the observed phenomena (Fig. 12). Once more significant differences could be detected in the rhythm of cellular divisions in the precursors of granulocytes and red cells.

The third series of experiments was aimed at quantitation of the reaction of the lymphocytic system.

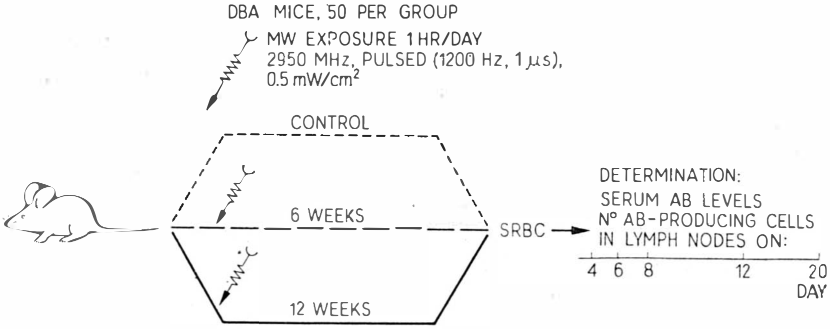
DBA MICE, 50 PER GROUP
MW EXPOSURE 1 HR/DAY
2950 MHz, PULSED (1200 Hz, 1 μs),
0.5 mW/cm²
CONTROL
6 WEEKS
12 WEEKS
SRBC
DETERMINATION:
SERUM AB LEVELS
N° AB-PRODUCING CELLS
IN LYMPH NODES ON:
4 6 8 12 20
DAY

Fig. 13. The experimental system used in the third series of experiments.

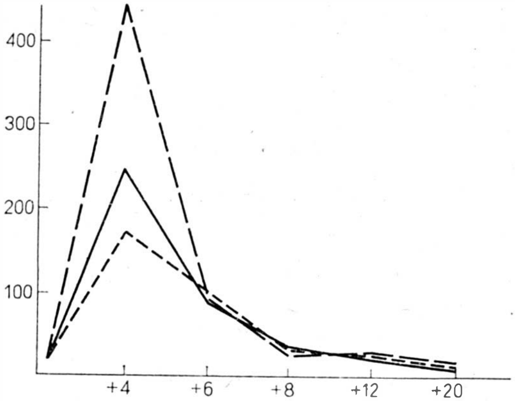

Fig. 14. The number of antibody producing cells in the lymph nodes of control and irradiated mice (direct Jerne's plaque technique).

Syngeneic mice were irradiated for 6 or 12 weeks, immunized with sheep red blood cells and the serum hemagglutinin level, as well as the number of antibody producing cells in lymph node homogenates, determined using Jerne's direct and indirect plaque techniques (9). The experimental system is presented in Figure 13, the results — in Figures 14 to 16. Differences between the control group and both irradiated groups in the course of the immunologic reaction are clearly seen. This indicates that the microwave exposure affected the lymphocytic system of immunocompetent cells. Additionally,

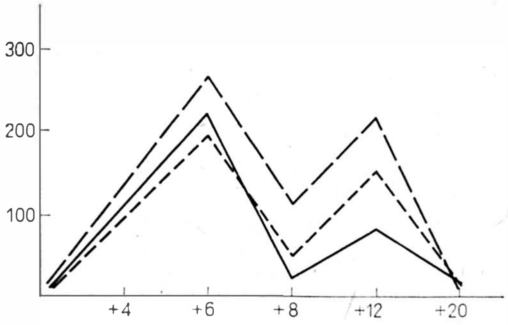

Fig. 15

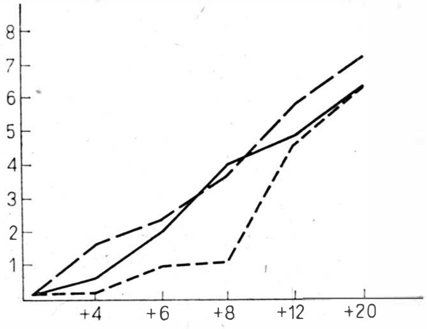

Fig. 16

Fig. 15. The number of antibody producing cells in the lymph nodes of control and irradiated mice (indirect Jerne's plaque technique).

Fig. 16. Hemagglutinins in the serum of control and irradiated mice.

it should be stressed that peripheral blood lymphocytes of long-term, low-dose irradiated rabbits undergo "spontaneous lymphoblastoid transformation" when cultured *in vitro* in a proportion dependent on the total exposure time (6). All these observations, as well as those of Stodolnik-Barańska (this volume) seem to indicate a peculiar susceptibility of the lymphocytes and the lymphocytic system to microwave radiation.

No explanation of the observed phenomena may be offered at this time. The most significant findings should, however, be pointed out:

1. Differences between CW and pulsed microwave effects at the same wavelength and average power density in strictly comparable exposure conditions were demonstrated by iron metabolism studies.

2. Differences between microwave effects on the circadian rhythm of mitoses of cells belonging to various hematopoietic cell lines were demonstrated; this may serve to stress the importance of taking into account the physiologic properties of cells, tissues and organs, when investigating microwave bioeffects and the danger of generalizations.

3. The above results and numerous reports in the literature point to the existence of easily demonstrable and easily quantified microwave effects on the lymphocyte and the lymphocytic system. It is the authors' feeling that this cell is a convenient model for further studies of microwave effects at the cellular level. Possibly reactions of the lymphocytic system could be used to develop a biologic comparative index to assess microwave bioeffects in various tissues and organs, as well as under various exposure conditions.

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HARMFUL EFFECTS OF MICROWAVE RADIATION ON THE BONE MARROW

K. Yagi, R. Ueyama, S. Kurohane, N. Hiramine, H. Ito and S. Umehara

IIIrd Department of Internal Medicine, Tokyo Medical College, Tokyo, Japan

During the second world war, the Japanese army studied the biologic effects of microwaves for use as a death ray and many harmful effects were observed (9), but all the results of the studies were destroyed by fire immediately after the end of the war. After the war, Inoue and Fujino (3) studied the effects of microwave radiation on peripheral blood cells. Umehara (11), one of the co-authors of this report, studied the biologic effects of microwave radiation on several organs of guinea pigs and reported that microwave radiation induced a serous allergic-like inflammation in many organs, such as the liver, lungs, kidneys, heart and gastrointestinal tract. These results were reported in "Nippon Acta Radiologica" in 1950.

On the basis of the results of the studies, Umehara recently speculated that microwave radiation might induce a serous inflammation in the bone marrow and result in aplastic bone marrow. In order to prove this speculation, the author performed an experiment to observe what changes occurred in the bone marrow after irradiating one femur of rabbits with microwaves (12).

It was proved by this experiment that an aplastic bone marrow developed after the microwave exposure. Furthermore, Ueyama designed an experiment to find out whether cortisone would prevent the development of aplastic bone marrow after the microwave exposure or not. These results are the subject of this report.

MATERIALS AND METHODS

Young white male rabbits weighing about 1.6 kg were used in these experiments (Tab. 1).

The microwave source was a 2450 MHz (12 cm) continuous microwave generator and the power density was 1.3 W/cm^2. The generator used was an ITO-200 Model therapy unit.

The rabbit was secured in a special wooden cage with a hole provided for one leg to be stretched out through it. The whole body except the left leg was completely shielded with a metal mesh. The distance between the antenna and the leg was 14 cm.

One irradiation session lasted 30 minutes and it was repeated 5 times a day for 7 consecutive days. The histologic changes in the irradiated bone marrow were examined during 6 weeks after the irradiation.

In the group in which the effectiveness of cortisone was observed, a 60-minute weak irradiation was made once daily for 2 weeks. 4 mg/kg of hydrocortisone were injected daily for 6 weeks from the beginning of the irradiation period or were terminated immediately after the exposures.

Table 1

Materials and Methods

1. Laboratory Animals
   Young White Male Rabbits weighing 1.6 kg
2. Microwave Generator
   (Microradar MR-200)
   manufactured by Itoh Electro Co.
   Output: 150 W
   Frequency: 2450 Mc/sec
   Wavelength: 12 cm
3. Irradiation Method
   Distance: 4 cm
4. Irradiation Time

	1st week			2nd week			3rd week			4th week			5th week	
Intensity	S	W	Rest	S	W	Rest	S	W	Rest	S	W	Rest	S	W
Exp. Time	5	25	30	5	25	30	5	25	30	5	25	30	5	25

Intensity: S (strong). Output: 150 W, Volt — 1700 V, Am — 200 mA
Intensity: W (weak), Output: 50 W, Volt — 1300 V, Am — 100 mA

The tissue temperature was measured by an electric thermometer.

Hematologic, histologic and histochemical studies were performed using routine techniques.

Table 2

Effect of microwaves on peripheral blood cells

	Hb %	RBC $\times 10^4$	WBC	Hemogram														Ht %
				N		E		Ba		Mo		Ly		L—Ly		S—Ly		
Pre Exp.	95	522	10 360	3 977	38.6	123	1.1	9	0.1	68	0.6	6 183	59.6	496	4.7	5 687	54.9	42
During Exp.	95	499	13 888	8 178	58.9	97	0.7	67	0.5	78	0.6	5 468	39.3	2 666	19.2	2 802	20.1	43
Post Exp.	93	464	12 237	6 608	54.0	68	0.7	39	0.5	69	0.6	5 453	44.5	4 387	35.8	1 066	8.7	45
1	95	485	12 227	6 984	57.1	133	1.1	36	0.3	230	1.9	4 844	39.6	2 841	23.2	2 003	16.4	48
2	95	507	10 481	5 830	55.6	178	1.8	80	1.8	43	0.4	4 492	41.4	1 837	16.1	2 655	25.3	52
3	96	520	11 661	5 650	51.2	223	2.0	135	1.2	96	0.8	4 949	45.8	1 746	15.8	3 203	30.0	52
4	98	542	11 950	6 369	53.3	250	2.1	79	0.6	113	0.9	5 139	43.1	1 527	12.8	3 612	30.3	52
5	103	552	12 500	5 380	43.0	357	2.8	121	1.0	174	1.4	6 468	51.8	1 149	9.2	5 319	42.6	55
6 weeks after Exp.	105	552	12 775	5 273	41.3	407	3.2	78	0.6	118	0.9	6 899	54.0	831	6.5	6 068	47.5	49

RESULTS

1. Changes in body weight: The body weight of the animals decreased gradually and was lowest from the 2nd to 4th week after the termination of the irradiation period. The average decrement of the body weight was 0.4 kg (Fig. 1).

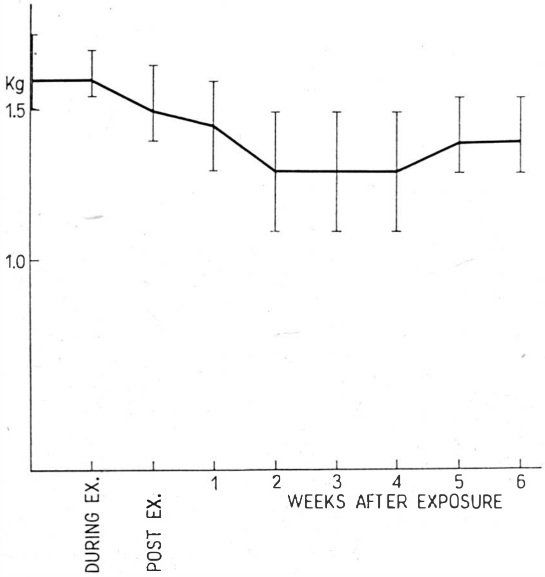

Fig. 1. Effect of microwaves on body weight.

2. Changes in tissue temperature: The temperature of the femoral tissue rose to 39°C within the first 5 minutes of irradiation and maintained a level of 42°C during the next 30 minutes (Fig. 2).

3. Changes in peripheral blood: A slight decrease in hemoglobin content and red cell count were found immediately after the irradiation period was terminated, but

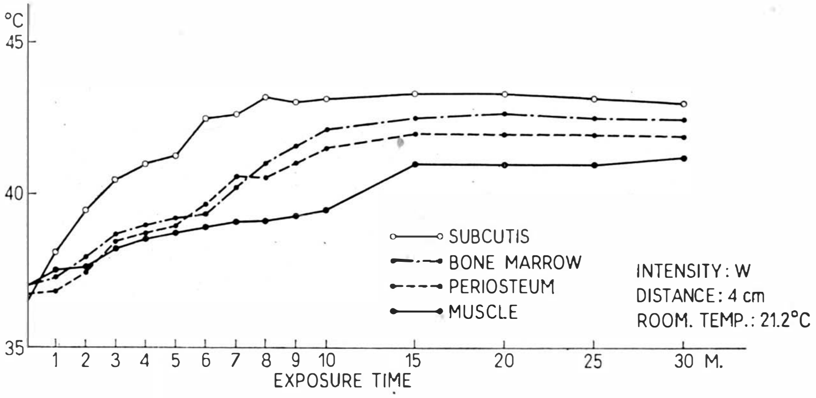

Fig. 2. Femoral tissue temperature during exposure.

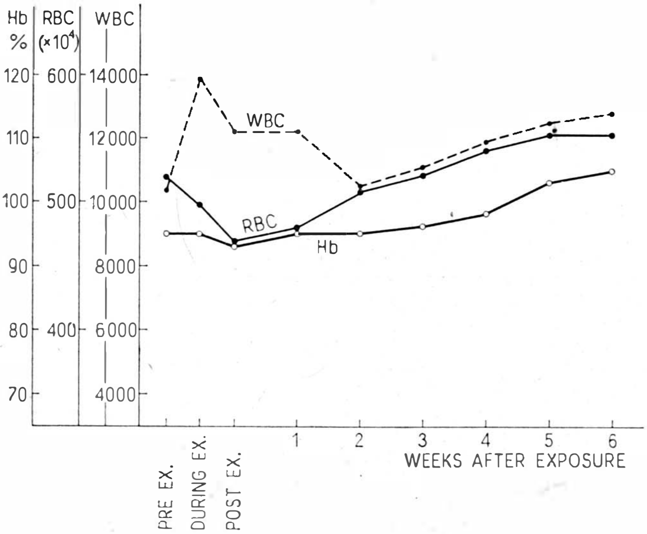

Fig. 3. Peripheral blood changes after exposure.

disappeared in the 4th to 6th week after the end of the irradiation period (Tab. 3, Fig. 3).

Moderate leukocytosis was observed during the irradiation (7) and slight leukocytosis continued for 6 weeks after the exposure was terminated. A moderate increase in neutrophilic leukocytes was seen during the irradiation and thereafter a slight neutrophilia continued during the whole course of the experiment. The lymphocytes, especially the small lymphocytes, decreased remarkably at the end of the irradiation (1, 6), but large lymphocytes increased to 900% of the initial value during the same period (Fig. 4).

Eosinophilic leukocytes also decreased during the irradiation, but increased to 400% of the initial value by the 6th week after the end of the irradiation period.

A progressive decrease of basophilic leukocytes was found. The changes in the monocytes were not significant.

4. Bone marrow findings.

a. Macroscopic findings: The colour of the bone marrow was fresh red and strong bleeding was seen during and immediately after the irradiation was terminated. The colour changed to yellowish red in the 1st to 3rd week after the end of the irradiation period. At that time, the bone marrow was jelly-like. The colour of the bone marrow changed further to gray in the 4th to 6th week after the irradiation period was terminated.

b. Histologic findings: The changes in the hemopoietic cells were not very remarkable the first 3 or 4 days after the irradiation was initiated (5). The most specific and characteristic finding at that time was the appearance of plasma-like substances coloured pinkish with hematoxylin-eosin staining. The plasma-like substances had a tendency to develop around the fat cells, though they were also found in the center of the parenchyma. This state was named "sand bay formation" by us. It was suggested that the plasma-like substances seemed to be an exudate (Fig. 5).

Seven days after the irradiation was begun, the exudate increased gradually in the parenchyma and surrounding fat cells. This finding was called "perilipocytic edema". The sinuses were filled with the plasma-like substance and dilated (Fig. 6). Degenera-

Table 3

Staining of the exudate, megakaryocytes and blood vessels

		During Exp.	Post Exp.	Time after Exposure						
				2—6 Days	1	2	3	4	5	6 Weeks
Exudate	H. E.	±	+	+++	+++	+++	++	++	+	±
	PAS	±	+	++	++	+	±	±	±	±
	Mucicarmine		+	++	+	+++	+	+	±	±
	Best's Carmine		—	—	±	±	++	±	±	
	Van Gieson's	±	++	++	+++	++	++	++	++	+
	Silver Nitrate	—	+	++	+	++	++	+++	++	±
	T. B. M.		++	++	++	+	—	—	±	—
	Azan Mallory's		—	—	±	±	++	+++	+++	++
Megakaryocytes	PAS	+	+	+	+	±	±	—	±	±
	Mucicarmine		—	—	—	+	±	±	±	+
	Best's Carmine		—	—	—	—	—	—	±	—
	Van Gieson's	+	++	++	++	+	+	+	—	±
	Silver Nitrate	+	+	++	+	+	+	+	++	++
Blood vessels	PAS	±	+	++	++	++	+	—	—	±
	Mucicarmine	+	—	—	—	—	—	—	—	—
	Best's Carmine			+++	+	±	—	±	—	—
	Van Gieson's	+	++	++	+++	++	++	++	+	++
	Silver Nitrate		—	+	+	+	++	+++	++	±
	Azan Mallory's	—	—	±	+	++	+++	+++	++	++

tion of the hemopoietic cells began to occur and bleeding into the parenchyma was seen. However, in some cases, a diffuse proliferation of hemocytoblasts was seen (Fig. 7). Vascular changes such as fibrinoid swelling and desquamation of the endothelium were observed.

2 or 3 days after the irradiation period was terminated, the hemocytoblasts and the fat cells decreased; this was associated with an increase of the exudate in the parenchyma. The cell arrangement of the parenchyma was disturbed, and degeneration of the hemocytoblasts and the blood vessels progressed. Karyorrhexis and vacuolization of the megakaryocytes were seen (Fig. 8). Follicular lymphoid cell infiltration became

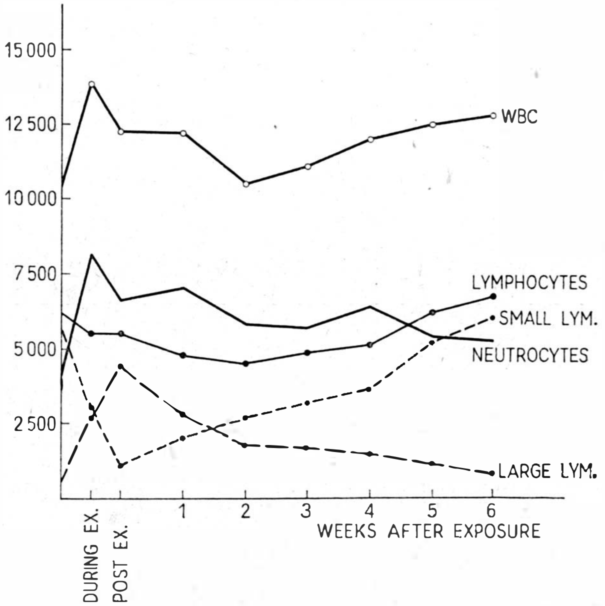

Fig. 4. Effects of microwaves on leukocytes.

more noticeable. Fibroblasts were found around the hemorrhagic and necrotic areas of the parenchyma.

In the 1st week after the end of the irradiation period, an increase in the exudate became more prominent and the fat cells decreased further. An overal reduction in cellularity was apparent and degeneration of the erythroid and myeloid cell was clearly seen. Degeneration of the blood vessels such as vacuolization also became more evident (Fig. 9).

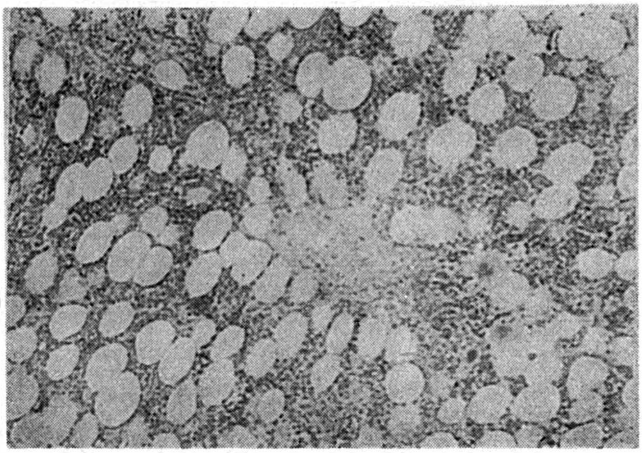

Fig. 5. Diffuse proliferative type. Diffuse proliferation of the hemocytoblasts is seen and plasma-like substances appear locally in the parenchyma. Irradiation 5 days, hematoxylin-eosin (×40).

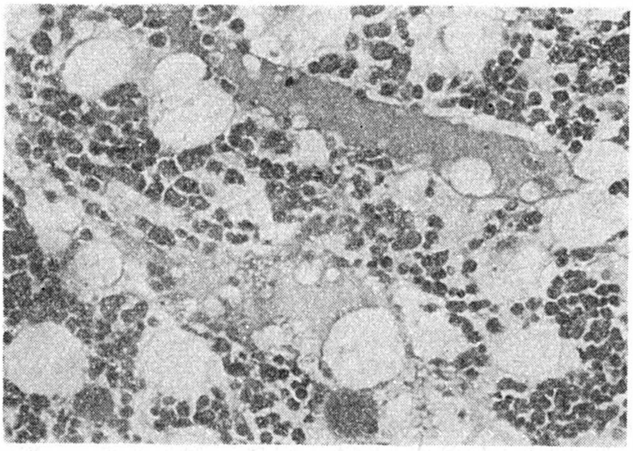

Fig. 6. The sinuses are filled with the plasma-like substances and dilated strongly. 3 days after irradiation, hematoxylin-eosin (× 120).

At the 2nd week, the fat cells disappeared due to an extreme increase in the exudate (Fig. 10). Degenerated parenchyma cells were scattered in the exudate like islands.

At the 3rd week, the exudative changes progressed further. Destruction and decrease of the parenchymal cells became more marked (Fig. 11). In some cases, partial fibrosis of the bone marrow was observed and completely fibrotic marrow was seen (Fig. 12).

At the 4th week, the exudate began to decrease and the fat cells began to appear again. However, the parenchyma cell decrease continued and severe degenerative changes were seen (Fig. 13). In some cases, aplastic bone marrow was seen, though little exudate remained between the fat cells.

In the 5th and 6th weeks, in some cases which showed remarkable exudation, distinct sinus wall thickening and plasmastasis in the sinus were seen. These sinus degenerations had a worm-like appearance (Fig. 14). However, in most cases, the exudate was absorbed and disappeared completely, while the fat cells increased progressively in place

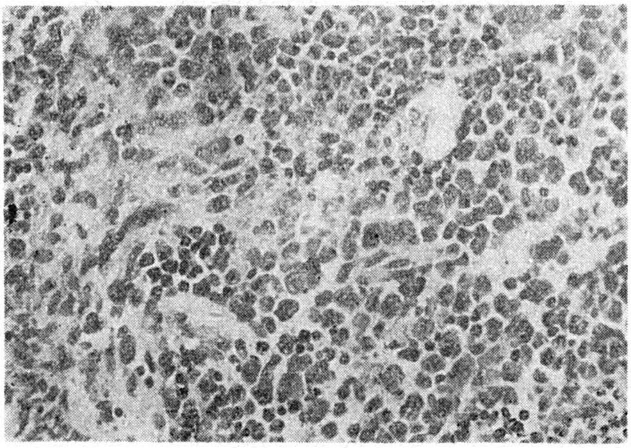

Fig. 7. Diffuse proliferation of the hemocytoblasts. Irradiation 7 days, hematoxylin-eosin (×120).

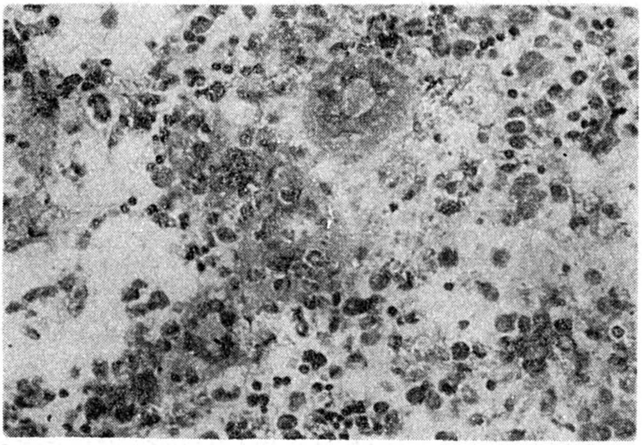

Fig. 8. Degeneration of the megakaryocytes. 3 days after irradiation, hematoxylin-eosin (×120).

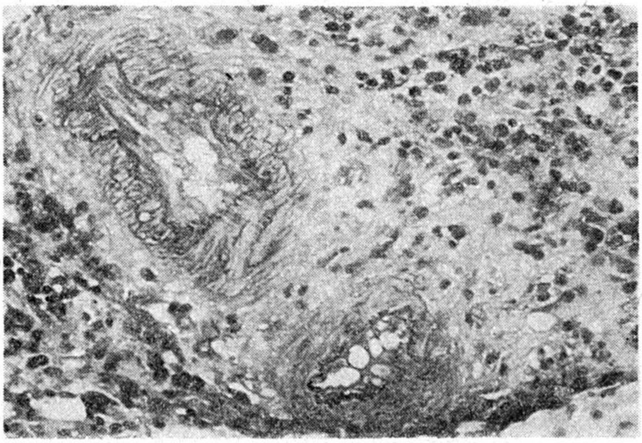

Fig. 9. Degeneration of the blood vessels and the plasma-like substances in the intravascular space. 1 week after irradiation, hematoxylin-eosin (× 120).

of the exudate. The parenchyma cells were destroyed and disappeared. Thus, completely aplastic bone marrow developed (Fig. 15). This aplastic bone marrow was almost the same as that found in human beings. Such completely aplastic bone marrow was found in 5 cases out of 7 in the 5th week and in 6 cases out of 9 in the 6th week.

However, in 2 cases out of 9 animals observed in the 6th week, slight regeneration of the hemocytoblasts was found (Fig. 16).

The fibrosis seen in the 3rd week after irradiation was not found in the bone marrow obtained in the 5th or 6th week.

c. Histochemical findings: In order to study the characteristics of the plasma-like amorphous substances in the parenchyma, blood vessels and megakaryocytes, the bone marrow preparations were stained by various methods, such as PAS, mucicarmine, Best's carmine, Van Gieson's silver nitrate, toluidine blue metachromasia at pH 3.5, Azan Mallory's and iron stainings (Tab. 3).

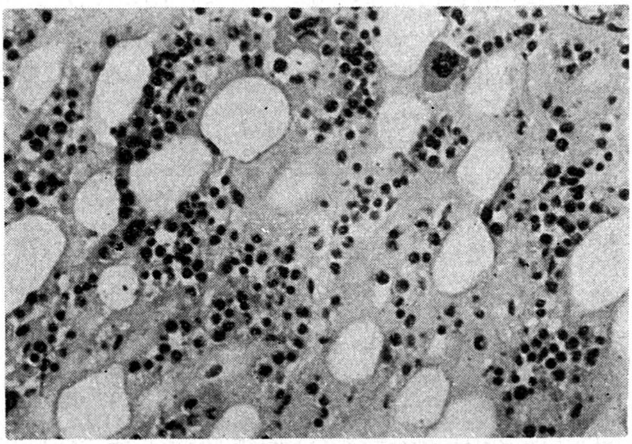

Fig. 10. So called "Gallert Mark" filled with the exudate. Parenchymal cells degenerāte and decrease. 2 weeks after irradiation, hematoxylin-eosin (× 100).

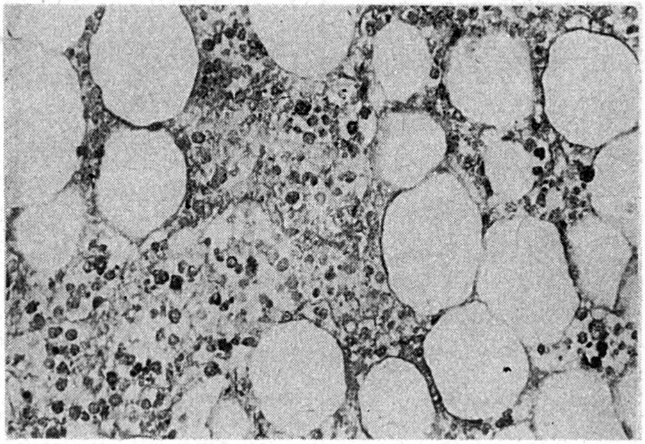

Fig. 11. The exudate is absorbed and the fat cells are increasing. Many degenerative cells and corpses of the cells are seen. 3 weeks after irradiation, hematoxylin-eosin (×120).

The plasma-like substance showed a positive reaction to PAS, with peaks within 1 week after the end of the irradiation period, and to TBM with a peak at the same time. Mucicarmine staining also became positive and showed a maximum in the 2nd week. From these findings, it was supposed that the plasma-like substance contained neutral and acid mucopolysaccharides. Therefore, the substance seemed to be an exudate which came from the blood serum due to an inflammation of the bone marrow.

The blood vessels also showed a positive reaction to PAS, Azan Mallory's and Van Gieson's stainings. A fibrinoid swelling was recognized in the blood vessels. From these observations, it seemed that the changes in the bone marrow after the irradiation were those of serous inflammation resembling allergic inflammation (2, 8).

The granulocytes and the megakaryocytes showed a positive reaction to PAS at the 1st week, but a very weak reaction from the 2nd week onwards and thereafter. These

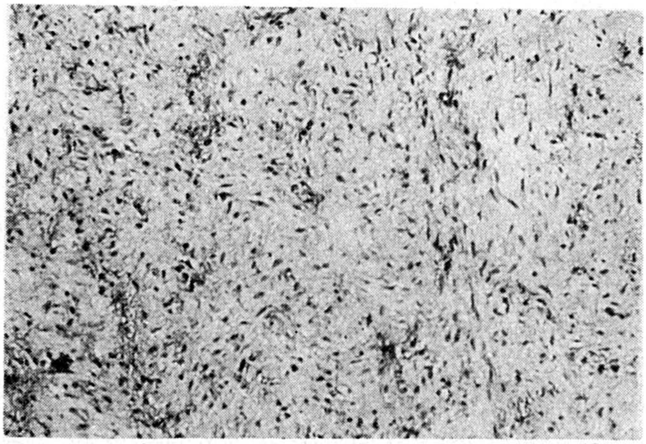

Fig. 12. Complete fibrosis. 3 weeks after irradiation, Azan Mallory's (×60).

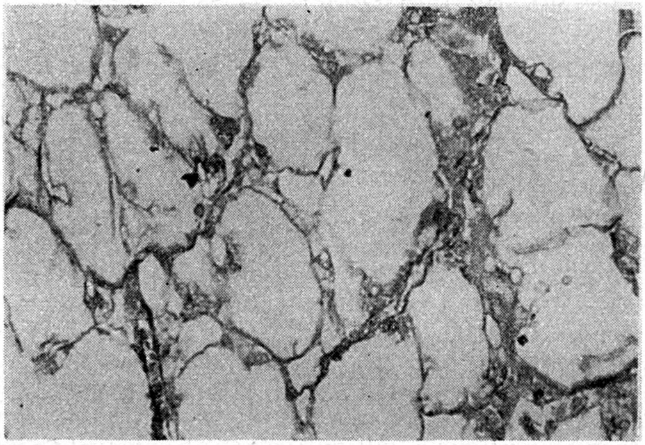

Fig. 13. Aplastic bone marrow. The exudate disappears and no parenchymal cells are seen. Notice the fat cells with irregular membranes torn off and elasticity lost. 4 weeks after irradiation, hematoxylin-eosin (× 120).

findings seemed to suggest that the degeneration of these cells progressed from the 2nd week.

The cells containing the iron granules increased from the 1st to the 3rd week. This means that destruction of the erythrocytes occurred mostly in this period.

d. Alkaline phosphatase reaction of the sinus wall: From the results of the studies mentioned above, it appeared that microwave irradiation induced certain changes of the sinocapillary wall of the bone marrow and a serous inflammation, resulting in aplastic bone marrow.

In order to prove this sino-capillaropathy, Kurohane, one of our co-workers, studied the changes of the sinus wall by alkaline-phosphatase staining and the India ink infusion method.

Normal bone marrow showed a distinct positive reaction to AP staining. After the

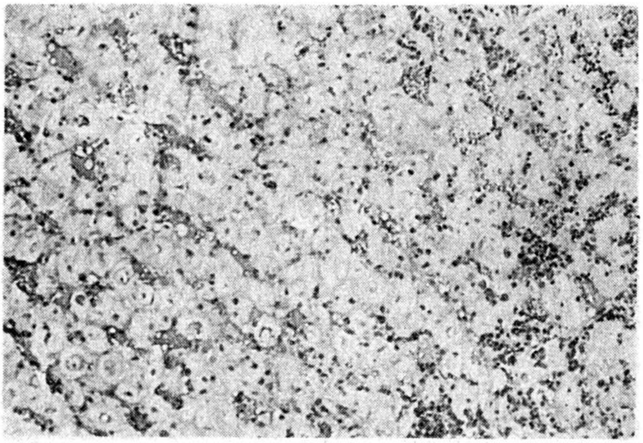

Fig. 14. Exudative changes are remarkable and plasma stasis in the sinuses is seen. 5 weeks after irradiation, hematoxylin-eosin (×120).

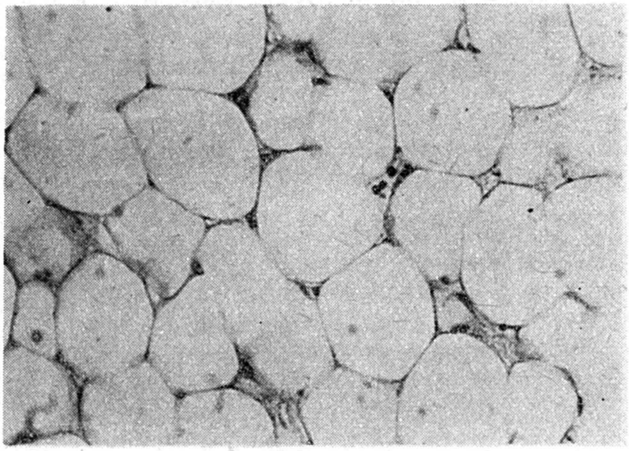

Fig. 15. A typically complete aplasia. The exudate and the hemocytoblasts disappear completely. The membranes of the fat cells become regular and show elasticity. 5 weeks after irradiation, hematoxylin-eosin (×120).

irradiation, the reaction decreased gradually. In the 2nd week, a weak reaction was still present, but thereafter the reaction was absent.

From the results of the studies, it was concluded that injuries of the sinus wall progressed after the irradiation, especially from the 2nd week.

5. Effects of cortisone on radiation-induced bone marrow changes: Ueyama (10), one of our co-workers, studied the effects of hydrocortisone on the changes of the bone marrow induced by microwave radiation.

In this experiment, 60 minutes of exposure to weak radiation was made once a day and continued for 14 days. The animals were divided into 3 groups, that is, a control group, a group treated daily with hydrocortisone from the beginning of irradiation and a group treated with hydrocortisone immediately after the irradiation period was terminated.

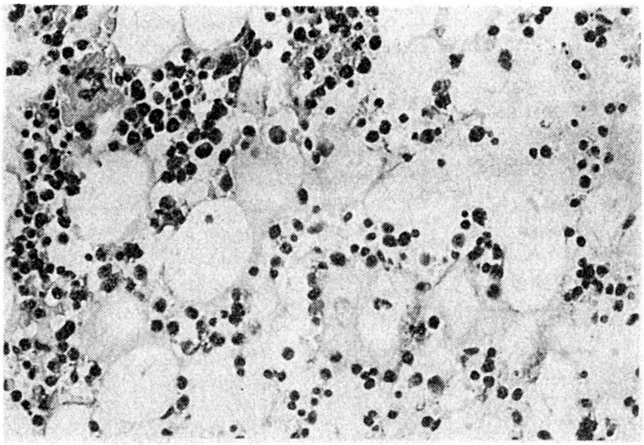

Fig. 16. The regenerative bone marrow. 6 weeks after irradiation, hematoxylin-eosin (×100).

In the control group, the exudative changes and destruction of the parenchymal cells occurred as mentioned above.

On the other hand, no such marked exudation occurred in the group treated with hydrocortisone from the beginning of the irradiation period and no changes were found in the parenchymal cells.

In the control group, aplastic bone marrow developed in the 3rd week after irradiation, but in the group treated with hydrocortisone, such an aplastic bone marrow did not develop. On the contrary, in some cases a proliferation of hemocytoblasts was found.

Even in the group treated with hydrocortisone immediately after the end of the irradiation period, exudative changes and degeneration of the parenchymal cells were very slight and aplastic bone marrow did not develop.

The results of the studies proved that bone marrow changes after irradiation consisted in serous inflammation which was suppressed by hydrocortisone administration.

DISCUSSION

In 1950, Umehara reported that microwave exposure produced a serous inflammation of many organs in guinea pigs, such as hepatitis, endo- or myocarditis, nephritis, pneumonitis, gastritis or even gastric ulcer. In that report he concluded that these changes might be caused by the harmful effects of microwaves on the endothelium of the capillary walls under rather low temperature. In the experiments reported here, it was proved that microwave radiation also caused sinus wall injuries in the bone marrow and induced a serous inflammation, resulting in aplastic bone marrow.

This indicates that microwave radiation has a clearly harmful effect on the bone marrow under certain conditions and aplastic anemia might be caused by an inflammation of the bone marrow rather than by stem cell failure (4).

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EFFECTS OF MICROWAVES ON THE CELL METABOLISM OF THE RETICULO-HISTOCYTIC SYSTEM

L. Miro, R. Loubière and A. Pfister

Faculty of Medicine in Montpellier-Nimes, Laboratory of Biological Physics.
Nimes Section, Nimes, France

From clinical and biological investigations of people exposed to microwaves, we found that an exposure for a long time at a low mean power density (from 0.1 to 0.2 mW/ /cm^2) produced subjective and objective disorders in a number of subjects.

In order to find out the source of these disorders, a first series of experiments was carried out with material to be described later. During 450 hours, mice, rats and rabbits were exposed to the action of continuous microwaves of 7 mW/cm^2 mean power density. During the experiment no modification in either the behaviour or appearance of the animals could be noted. At the end of this experiment all the animals were decapitated and anatomo-pathologic studies of all their organs were made. No macroscopic or microscopic alteration of these organs could be noted; we found only a hyperplasia of the spleen and liver of these animals which seemed to indicate a possible stimulation of their reticulo-histocytic system.

With the aim of investigating this effect in more detail we carried out a systematic study on the liver, spleen and thymus cell metabolism of mice exposed to microwaves.

MATERIAL AND METHODS

Exposure to microwaves was carried out using a pulse-modulated emitter with the following characteristics:

— wavelength: 10 centimeters
— frequency: 3.105 MHz ± 15 MHz
— pulse width: 1 ms
— duty cycle: 50 Hz
— emitting peak power: 400 W
— emitting mean power: 20 W.

The microwaves were emitted from a horizontal horn and the exposed animals were situated in the far field where the mean power density was about 2 mW/cm^2.

All the experimental animals (Fig. 1) were situated in an anechoic chamber 3 meters in diameter, made of absorbant Eccosorb 330 F.R. sheets, the power measurement being carried out with a Sperry field meter.

The experiments were carried out on 40 male mice of "Swiss" pure strain, weighing from 26 to 30 grams. Each mouse was identified and matched with another of the same weight to haft a gram. Thus, two identical groups were constituted, one being used as a control group and the other exposed to microwave radiation.

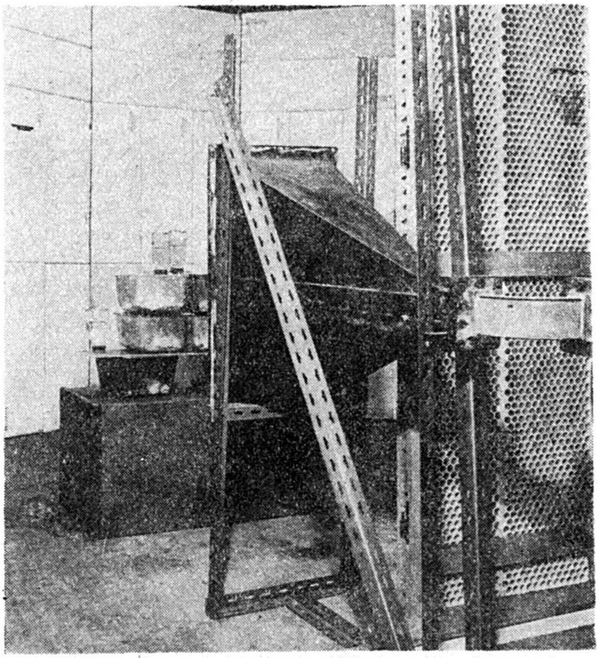


Fig. 1. For explanation, see text.

The experimental group was continuously exposed during 145 hours to microwave radiation, the control group being kept under exactly the same conditions of life in another room throughout all the experimental period;

The animals were not restrained and received water and food at will.

The weight of each animal was recorded daily as well as its behaviour: we also controlled the central temperature of the animals, maintaining it stable so that it did not vary more than half a degree centigrade.

After the exposure we injected all the animals intraperitoneally with a methionine ^{35}S solution in a dose of 2.5 μCi per gram of body weight, and each of the groups was returned to its appropriate surrounding, one normal, the second microwave irradiated. 15 hours after the injection, all mice were decapitated and an autopsy was made immediately. The spleen, liver and thymus were set apart and fixed in "Bouin liquid", then treated according to the classical anatomo-pathologic techniques. However, an inclusion in paraffin was performed, the homologous organs of each matched animal (the control and the experimental one) being included in the same block. Thus on the same microscopic preparation one could find side by side a view of an experimental and a control organ having exactly the same thickness and processed in the same manner.

Each preparation was then covered with nuclear emulsion Ilford (G5), dried and preserved in a cold and dark place for 15 days, and then processed.

The optical density obtained after the reduction of the silver salt by the 167 keV beta radiation of ^{35}S methionine was measured with a "Lison histophotometer" coupled to a Reichert-Zetopan microscope. Comparative measurements were made on the homologous preparations by the examination of corresponding sites; each value is the statistical result of 30 measurements.

By another method hematein-eosin-safran staining was performed simultaneously on a preparation coming from the same paraffin blocks as those from which the preparations for histoautoradiography were made. So it was possible to compare the classical anatomo-pathologic aspect of the control and exposed organs and to locate histologically the incorporated ^{35}S methionine.

RESULTS

During irradiation no difference between the behavior of control animals and exposed animals was noted, and weight curves did not show any modification in the initial weight.

At the time of autopsy, three matched animals were rejected from the experiment because they developed certain organic lesions without clinical manifestations and these might have affected the incorporation of amino acids.

As the end result 17 matched animals were studied.

The classical anatomo-pathologic examinations permitted the following conclusions:

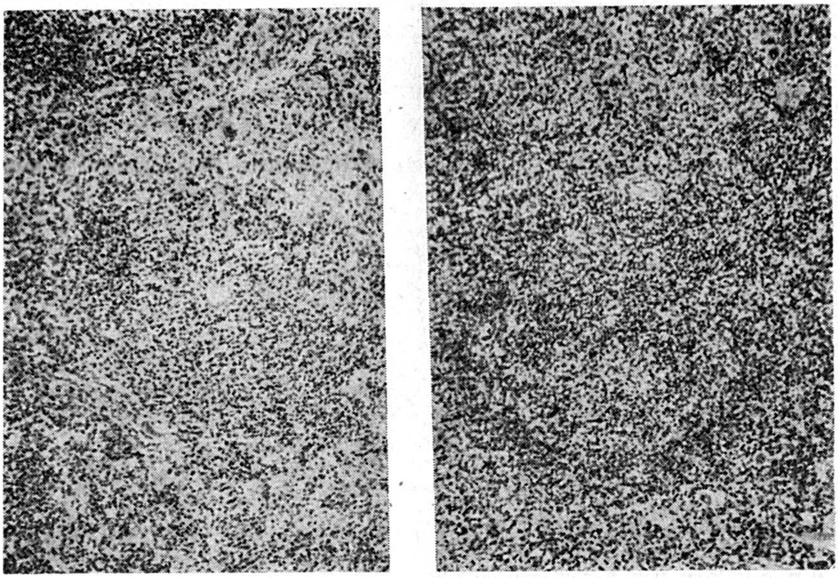
Spleen. There was a greater extension of germinative centers in exposed animals than in controls; the cellular density increased and lymphoblastic cells were more numerous (Fig. 2).

In lymphoid areas the lymphocytes were abnormally distributed in sheets; foci of eosinophil cells and large numbers of reticular cells were found.

In the red pulp many of the same cells could be seen completing the picture of spleen hyperplasia.

Disorganization of the hepatocytic structure, and enlargement of the hematopoietic islet were also observed.

Liver. An increase of the reticular and histocytic cells of mesenchymatic origin in the Disse spaces was noticed (Fig. 3).



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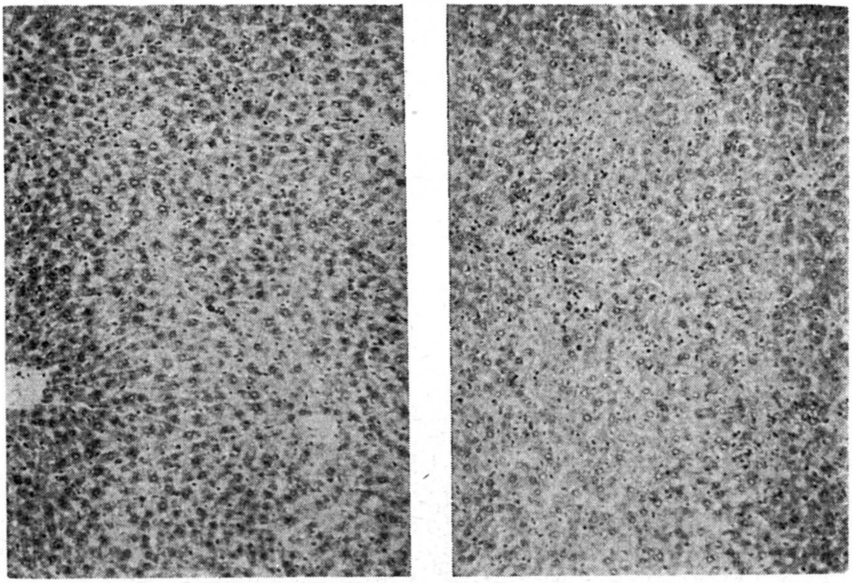


Fig. 3. For explanation, see text.

Thymus. The cellular density of cortical areas was marked in the subcapsular zones by a great number of lymphoblasts and abundancy of reticular cells.

This reticulohistiocytic hyperplasia was confirmed by the dynamic examination of these organs, i.e. the study of ^{35}S methionine incorporation. The optic densities of hepatic preparations and the homologuos splenic and thymic zones were measured and compared between control and exposed animals.

For each group a good gaussian distribution of results was obtained which permitted a statistical analysis to be made using Student's "t" test.

In Tables 1, 2, 3, 4, for each pair of animals the average measurements of optic density, the values of "t" and the degree of significance are given.

For the germinative centers and lymphoid zone of the spleen, liver and thymus, both in the cortical zone and in the medulla, we observed in all the exposed animals a very clear increase in the rate of incorporation of the tagged aminoacid as compared to the control animals (Fig. 4). This difference is very highly significant in all cases ($p < 0.001$). The magnitude of the increase obtained is variable and seems to be connected with an individual factor.

Only in the red pulp of the spleen could a wider range of results be seen: if in most cases (88% of animals) the ^{35}S methionine incorporation is higher in exposed mice, the statistical studies show that the average difference is very significant ($p < 0.001$) only in 12 animals and that the degree of significance varies between 0.001 and 0.005 in 3 animals; in at least 2 cases the average difference is not significant.

At the end of the first part of the study we noticed an increase of ^{35}S methionine incorporation in the spleen, the liver and the thymus of mice exposed to microwave radiation.

These results pose three kinds of problem:
- — the significance of the optical density measured histophotometrically,
- — the limitations of the method used,
- — the overall possible interpretation of the results.

Table 1

Incorporation of ^{35}S methionine into the germinative centers of the spleen (measurements of optical densities)

Pair of animals No.	Averages in animals		t	Degrees of significance
	exposed	controls		
1	19.25	13.88	12.17	$0.001 > p$
2	19.00	14.63	11.64	$0.001 > p$
3	13.50	11.75	3.78	$0.001 > p$
4	19.76	8.63	11.00	$0.001 > p$
5	19.20	9.56	18.00	$0.001 > p$
6	32.00	21.00	10.67	$0.001 > p$
7	26.40	18.00	16.50	$0.001 > p$
8	21.00	9.33	16.31	$0.001 > p$
9	30.93	18.73	21.07	$0.001 > p$
10	29.00	18.83	20.62	$0.001 > p$
11	27.63	22.93	8.62	$0.001 > p$
12	21.40	17.56	10.69	$0.001 > p$
13	25.36	18.76	6.16	$0.001 > p$
14	23.43	21.06	4.83	$0.001 > p$
15	28.90	26.36	4.23	$0.001 > p$
16	33.86	26.36	10.70	$0.001 > p$
17	28.20	23.33	8.10	$0.001 > p$

Table 2

Incorporation of ^{35}S methionine into the lymphoid zone of the spleen (measurements of optical densities)

Pair of animals No.	Averages in animals		t	Degree of significance
	exposed	controls		
1	16.50	13.33	4.50	$0.001 > p$
2	8.85	6.90	5.81	$0.001 > p$
3	8.80	6.70	4.66	$0.001 > p$
4	11.33	3.83	7.07	$0.001 > p$
5	10.06	6.03	9.60	$0.001 > p$
6	19.33	15.00	7.21	$0.001 > p$
7	17.00	11.00	12.14	$0.001 > p$
8	11.40	4.56	13.00	$0.001 > p$
9	18.50	12.33	6.02	$0.001 > p$
10	18.13	12.00	14.46	$0.001 > p$
11	13.03	10.83	8.50	$0.001 > p$
12	11.83	9.17	12.60	$0.001 > p$
13	15.76	11.96	11.27	$0.001 > p$
14	14.66	13.73	9.52	$0.001 > p$
15	20.63	16.26	9.23	$0.001 > p$
16	23.46	16.26	13.28	$0.001 > p$
17	16.03	12.70	9.68	$0.001 > p$

Table 3

Incorporation of ^{35}S methionine into the spleen red pulp (measurements of optical densities)

Pair of animals No.	Averages in animals		t	Degree of significance
	exposed	controls		
1	32.10	23.56	7.77	$0.001 > p$
2	15.89	14.21	2.10	$0.05\ p > 0.02$
3	15.00	15.53	0.70	insignificant
4	22.53	9.00	24.00	$0.001 > p$
5	16.93	12.13	6.00	$0.001 > p$
6	33.00	34.00	0.67	insignificant
7	32.80	28.00	2.46	$0.02 > p > 0.01$
8	22.90	9.50	15.20	$0.001 > p$
9	32.86	27.26	4.44	$0.001 > p$
10	28.90	20.53	12.96	$0.001 > p$
11	22.23	20.26	5.18	$0.001 > p$
12	18.26	16.16	3.48	$0.001 > p$
13	30.36	27.46	3.76	$0.001 > p$
14	25.30	23.73	3.07	$0.01 > p\ 0.01$
15	31.43	26.70	7.70	$0.001 > p$
16	35.10	26.70	12.27	$0.001 > p$
17	26.83	23.26	6.81	$0.001 > p$

Table 4

Incorporation of ^{35}S methionine into the liver (measurements of optical densities)

Pair of animals No.	Averages in animals		t	Degree of significance
	exposed	controls		
1	16.46	13.06	6.12	$0.001 > p$
2	13.73	9.66	8.02	$0.001 > p$
3	13.60	11.36	4.75	$0.001 > p$
4	13.66	6.36	12.89	$0.001 > p$
5	13.66	9.10	6.66	$0.001 > p$
6	18.53	8.60	15.11	$0.001 > p$
7	14.46	11.46	5.07	$0.001 > p$
8	14.50	7.03	15.36	$0.001 > p$
9	15.53	9.63	12.36	$0.001 > p$
10	15.03	9.83	13.00	$0.001 > p$
11	17.33	12.16	14.60	$0.001 > p$
12	20.93	18.48	6.21	$0.001 > p$
13	31.76	28.93	4.12	$0.001 > p$
14	17.20	11.60	7.88	$0.001 > p$
15	26.30	21.73	4.52	$0.001 > p$
16	24.93	12.93	30.60	$0.001 > p$
17	24.72	21.30	7.96	$0.001 > p$

Table 5

Incorporation of ^{35}S methionine into the thymus (measurements of optical densities)

Cortical zone

Pair of animals No.	Averages in animals		t	Degree of significance
	exposed	controls		
2	24.70	21.80	5.00	$0.001 > p$
4	20.56	8.65	26.71	$0.001 > p$
5	18.46	10.40	23.79	$0.001 > p$
6	17.23	10.13	14.13	$0.001 > p$
7	15.83	11.53	10.14	$0.001 > p$
8	15.16	10.40	11.24	$0.001 > p$

Medullar zone

Pair of animals No.	Averages in animals		t	Degree of significance
	exposed	controls		
2	14.43	10.60	11.44	$0.001 > p$
4	11.53	5.50	17.48	$0.001 > p$
5	12.40	6.13	13.36	$0.001 > p$
6	12.26	6.66	15.77	$0.001 > p$
7	9.93	6.83	9.81	$0.001 > p$
8	10.60	6.93	10.15	$0.001 > p$

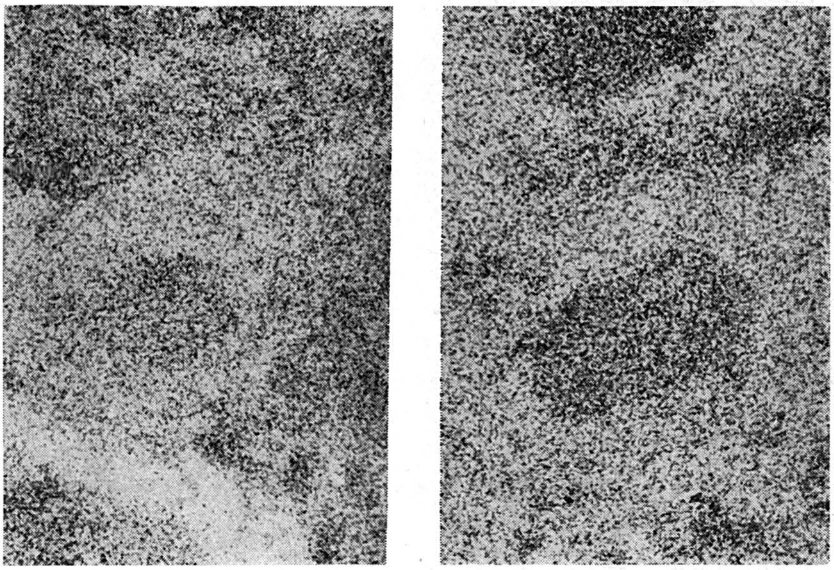


Fig. 4. For explanation, see text.

The technical protocol of our experiment allows us to give an answer to the first question. It may be demonstrated that, by using the histologic technique described, 91 to 97% of the radioactivity is due to the radiation from sulphur-35 of the methionine incorporated into a protein. The increased radioactivity observed in the mice exposed to microwave radiation is in conformity with an increase in protein synthesis by hepatic, thymic and splenic cells.

This is not a simple slowing down of the protein metabolism rate, but a real increase in the synthesis itself. In fact, in view of the relatively long time (15 h) which elapsed between the amimoacid administration and the sacrificing of the animals, we may consider that a steady metabolic state was established.

Finally, having included in the same paraffin block the organs of the matched mice, it was not possible to determine the differences between the optic density of the two preparations. Indeed these strictly underwent the same autoradiographic technologic processing: their thickness was the same, they were covered with the same emulsion film and the exposure time was the same.

The discordant results obtained in the red pulp could be explained by its anatomic nature: indeed, it is composed of many blood vessels. The radioactivity of this area depends not only on the Billroth strand, but also on the blood contained in sinusoid capillaries and venous sinuses. This fact explains why the blood radioactivity is modified according to the spleen contraction state at the moment of decapitation.

The limits of the method used result essentially from the choice of the labelled radioactive marker: the ^{35}S methionine indicates in fact only the protein cellular synthesis. All the cells contain sulphur proteins. This method does not allow differentiation of the histologic type of cells whose protein metabolism is increased. The resolution of histoautoradiographic methods does not allow by itself such a distinction. Therefore it is necessary to compare the hematein-eosine-safran stained preparation and the homologous autoradiographic preparation, each one coming from the same paraffin block. In this way we may demonstrate that the zone where the incorporation of ^{35}S methio-

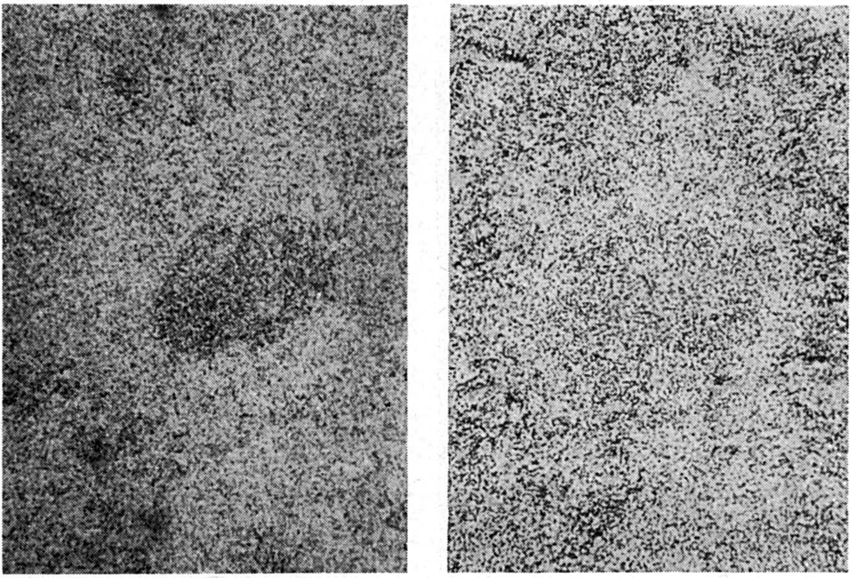


Fig. 5. For explanation, see text.

nine is increased corresponds to that zone where an increase in reticular and histiocytic cells is noted. Thus, in the spleen the more active zones in histoautoradiographic preparations are localized in the middle of germinative centers where a greater number of cells, especially lymphoblastic cells, is present (Fig. 5).

In the same way for the thymus a correlation can be made between the presence in the subcapsular zone of a large number of lymphoblasts with abundance of reticular and histiocytic cells and the existence in this zone on histoautoradiographic preparations of a darker strip than the remainder of the preparation.

In this way we were able to demonstrate histoautoradiographically an increase in protein synthesis in the zone where a histologically histocytic hyperplasia is noted.

CONCLUSION

In the actual state of our research we may conclude that the continuous exposure of mice for 160 hours to microwave radiation induces a great increase in protein synthesis in the liver, thymus and spleen. This was observed in zones where reticular hyperplasia was demonstrated by classical anatomo-pathologic methods.

In order to confirm or invalidate this effect of microwave radiation on the reticulo-histocytic system, it will be necessary to use a radioactive labelled product having a specific affinity for this system, such as colloidal gold-98 or a denatured iodine-125 albumin complex.

ARE MICROWAVES TERATOGENIC?

R. Rugh, E. I. Ginns, H. S. Ho, and W. M. Leach

Division of Biological Effects, Bureau of Radiological Health, Food and Drug Administration, United States Public Health Service, Rockville, Maryland, U.S.A.

INTRODUCTION

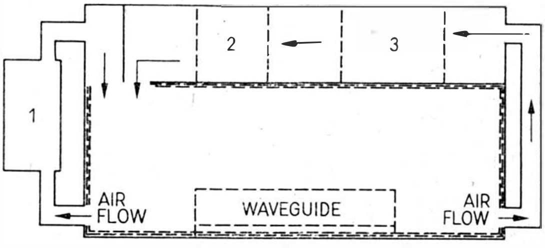
Accurate and reproducible dosimetry is proving to be a most important prerequisite for significant biological experimentation with microwave radiation. Since a dose-biological effect relationship should be established with experiments where the absorbed dose can be described, we have developed in our laboratory a waveguide irradiation facility that permits the precise determination of the total energy absorbed by a freely moving small living animal. The energy absorbed by an animal is dependent upon the geometry, size, orientation, and complex dielectric constant, and very possibly also upon such biological variables as hydration state, age, and endocrine status of each animal. Thus, two animals exposed to the same forward power of microwaves would most probably not absorb the same amount of energy in the same amount of time.

The extent of heat stress in animal systems during microwave irradiation has been evaluated by several workers. Haines and Hatch (3) as well as Belding and Hatch (1) proposed that heat loss and heat gain due to convection, the subject's metabolic rate, and the heat gain due to radiation, all contribute to the load experienced by a subject in the microwave field. In an effort to describe quantitatively the physiologically stressed state of a standard man in a microwave field, Mumford (5) derived values for the Heat Stress Index as a function of the Temperature Humidity Index (THI) and power density. Using rabbits, dogs, mice, and rats, Deichmann (2) further investigated the relationships between an animal's survival in a microwave field and the temperature, humidity, and air flow in the environment. These studies have shown that environmental conditions can influence the extent of stress upon any animal in a microwave field. Therefore, meaningful microwave biological effects data must be obtained from exposure situations where the environmental variables have been recognized, defined, and included in the dosimetric data. Our facility takes environmental variables into account to determine the integral absorbed dose of each animal, since it is the absorbed dose rate and dose that is of biological significance.

MATERIALS AND METHODS

Irradiation apparatus:

A detailed description of both the dosimetric and environmental parameters of our irradiation facility has been presented previously by Ho, Ginns and Christman (4). A chamber surrounding the waveguide permits the control of temperature, relative humidity, and air flow past the animal during exposure to microwave radiation. This chamber is shown schematically in Figure 1. The environment within the chamber is obtained by mixing two air streams — one that has been cooled and dehumidified, and



ENVIRONMENTAL CHAMBER
1. AIR CONDITIONER
2. HEATER
3. HUMIDIFIER

Fig. 1. Schematic drawing of the waveguide irradiation apparatus with controlled temperature and relative humidity environment. Conditioned air is drawn through the waveguide by means of a vacuum system.

one that has been heated and humidified. The air temperature is measured with a protected thermocouple probe located at the center of the chamber just above the waveguide. The range of relative humidity (measured with a membrane hygrometer at the air inlet of the waveguide) that can be obtained within the chamber is 25 to 70 percent ± 1.5 percent over the temperature range of 15 to 40°C, ± 0.5°C. Using the following equation by Mumford (5):

$$\mathrm{THI} = 1.44\ \mathrm{T} + 0.1\ \mathrm{RH} + 30.6$$

(where T = temperature in °C; RH = relative humidity) the environmental chamber provides a range of THI from 55 to 95. The temperature- and moisture-conditioned air within the chamber is drawn through the waveguide by a low-pressure (vacuum) system attached to one end of the waveguide.

The microwave generator provides up to 100 watts of continuous wave power at 2450 MHz. Within the waveguide the test animal is free to move within a holder (4.30 × 4.50 × 2.15 inches) made of low-loss materials (polyethyelene and styrofoam), which accounts for a 40 percent loss of forward power by reflection and absorption. Holes in the ends of the holder permit air flow past the animal.

The total amount of microwave energy absorbed by the animal is determined without perturbing the microwave field interacting with the irradiated animals. The forward, reflected, and transmitted powers are measured by power meters. The voltage output from each of the three power meters is fed into an integrator. Each of the power readings is integrated with respect to time and the integral dose can subsequently be calculated. The terms which describe dosimetric quantities are as follows:

Exposure rate: Incident power density (mW/cm^2) of an electromagnetic wave.

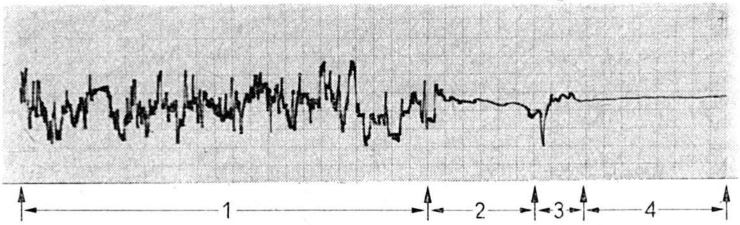
Integral dose rate: Time rate of absorption of electromagnetic energy (watts) by the complete biological target.

Integral dose: Total amount of electromagnetic energy (joules or calories) absorbed by the complete biological target.

Average dose: Integral dose per unit weight of the animal (joules/g or cal/g).

Distributed dose rate: Time rate of absorption of microwave energy per unit mass (W/kg or W/g). It is usually non-uniform in biological bodies even though the incident power density (exposure rate) may be uniform.

Since the animal is free to move within the holder during exposure in the waveguide, the reflected and transmitted powers are constantly varying. A typical pattern of reflected power variation during an exposure is illustrated in Figure 2. The ordinate



Activity Indicator
CF_1 mouse in an intense microwave field
(chart speed: 0.5 mm/sec)
Phase 1 Transition from unstressed state to stressed state
Phase 2 Fatigued and labored movement
Phase 3 Convulsive movement
Phase 4 Death

Fig. 2. Tracing of power reflected from an unanesthetized animal. These traicings provide a monitor of animal movement. Four phases of animal activity can be defined, as indicated on the chart.

corresponds to the voltage output from the power meter. The power variation can also be used as an "activity indicator" of the animal during exposure. It provides a means of investigating the sensitivity of an animal to both environmental and dosimetric (e.g., dose rate) parameters for which lethality is the biological endpoint. Death of the irradiated animal can be determined and the average integral or absorbed dose to death can be calculated.

Biological materials: Mature CF_1 white mice, 25—30 g, were used in these experiments. Females were timed-mated for the fetal studies, so that 8.5-day gestation stages were provided for microwave irradiation. Gestation day 8.5 is known to be particularly sensitive to ionizing radiation with respect to anomaly production. Some pregnancies were allowed to come to term, but most were terminated at 18 days to examine whole litters before the mother had an opportunity to destroy any of her malformed young, which is common practice for the mouse. Thus, in those graphs depicting fetal studies each point represents an entire litter, categorized as to percentage of anomalies, resorptions, etc. The following data represent the beginning of studies designed to compare the effect of ionizing and microwave radiations on the fetus. Such a comparison is of interest since ionizing radiations involve little or no rise in body temperature, whereas microwave radiation can involve substantial body heating.

EXPERIMENTAL RESULTS AND DISCUSSION

The irradiation of pregnant mice was performed with a forward power of 7.37 watts, constant temperature of 25°C and relative humidity of 50 percent, with variable exposure durations up to a maximum of 5 minutes. The THI calculated for these environmental conditions was 71.6. Prior to the initiation of irradiation, each mouse was acclimatized to this environment for 30 minutes. The average dose varied between approximately 3 and 8 cal/g. As can be seen in Figure 3, the average dose for lethality of adult male mice at a THI of about 70 is 12 cal/g (experimental conditions: forward power, 6.94 watts; variable temperature and relative humidity; duration of irradiation until death, as shown in Figure 3). Differences in response to microwave radiation are expected because of such factors as activity, sex, state of hydration, age and health status; and both integral dose rate, and dose distribution in the animal. These differences

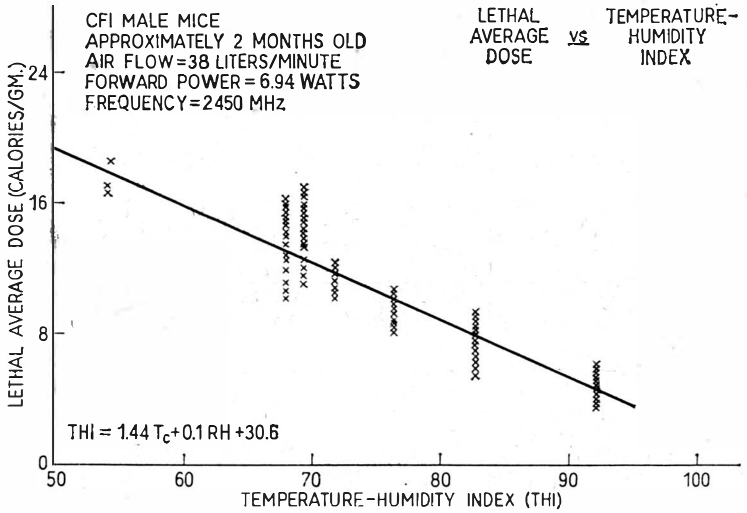


Fig. 3. The relationship between average dose to lethality of male mice and the temperature-humidity index (THI). Each point represents a single exposed animal. The THI formula and other experimental conditions are shown in the Figure.

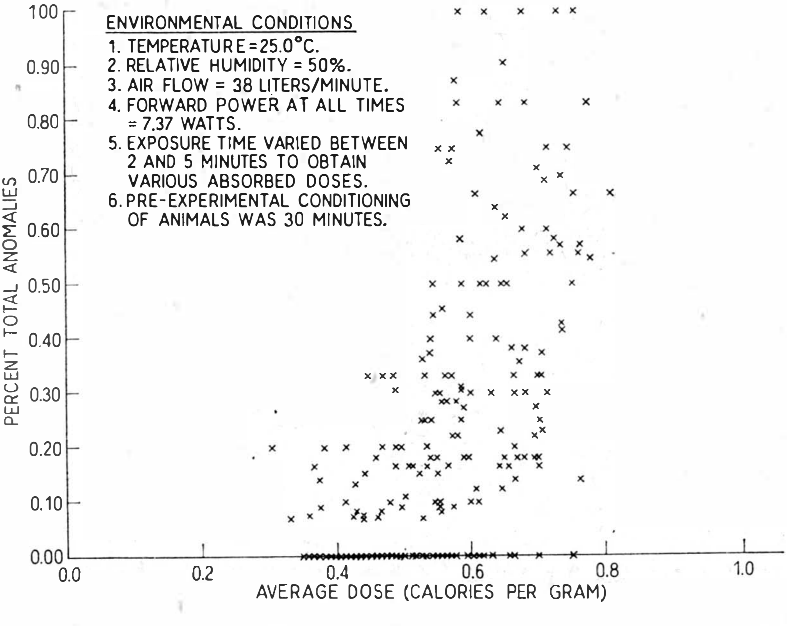


Fig. 4. Total observed fetal anomalies from microwave exposure. Each point represents the fraction of anomalous offspring in each irradiated litter, and is expressed as a percent of the litter. Environmental exposure conditions are as stated.

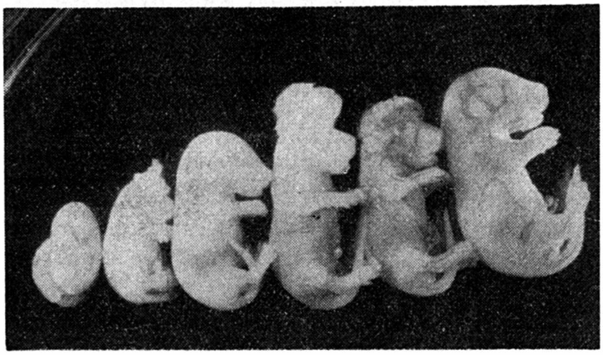


Fig. 5. Variety of anomalies obtained from various litters which had been exposed to microwave radiation. From left to right: Dead fetus still attached to placenta. Dead fetus with almost anencephaly. Apparently normal but stunted fetus. Normal sized fetus but with pronounced exencephaly. Ice-pack type exencephaly, with circulatory stasis. Apparently normal fetus with circulatory stasis.

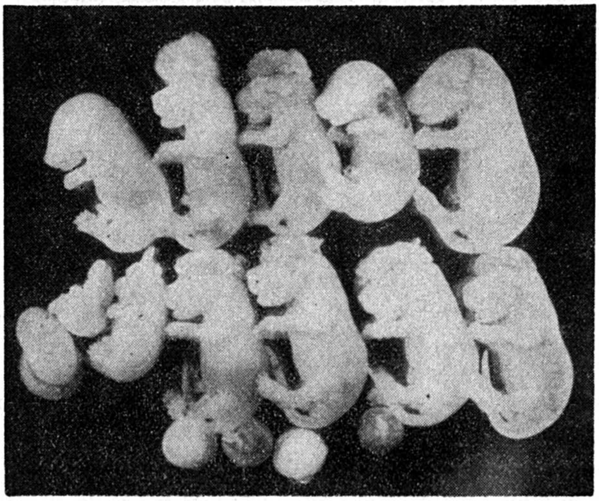


Fig. 6. Anomalies produced by microwave irradiation of CF_1 mice on their eighth day of pregnancy, showing: Resorptions (three examples). Dead fetuses (three examples), lower left. Exencephalies of various degrees (six). Stunting — (two examples); apparently normal topographically. Normal (one example) upper right.

prevent direct comparison of the data in Figure 3 with the radiation absorbed by the pregnant mice. However, we concluded that the doses to pregnant mice were moderately to severely stressful.

Figure 4 shows total observed anomalies among fetuses exposed to microwave radiation. Each point refers to the proportion of anomalous fetuses observed in each dissected litter, and is expressed as a percent of the total number per litter. Resorptions, dead, stunted, and malformed fetuses were scored as anomalous. Examples of these types of anomalous fetuses are shown in Figures 5 and 6. Such effects are distinct from immediate effects of microwave radiation on the fetus. Figure 7 shows two

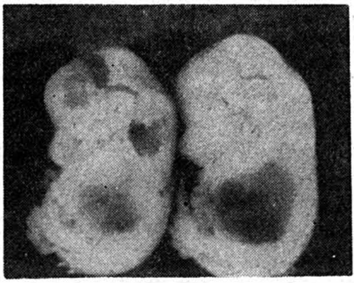


Fig. 7. Appearance of two mouse fetuses at day 15 of gestation after microwave irradiation of the mother. Fetuses were removed within 5 minutes after cessation of exposure to acute sublethal dose. Note hematomas throughout the body, and particularly in the head region.

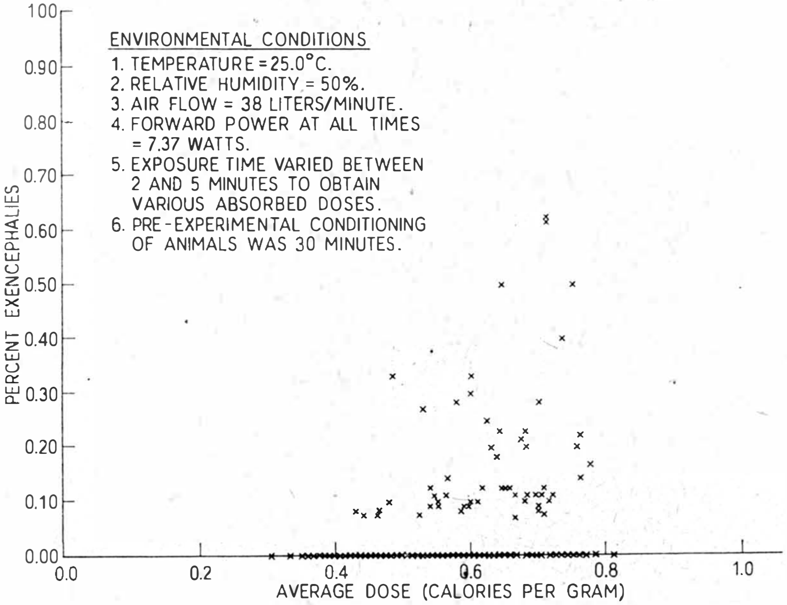


Fig. 8. Incidence of exencephaly in litters exposed to various average doses of microwave radiation. Each point represents the exencephaly in individual litter. Environmental exposure conditions were as indicated on the graph.

fetuses removed at day 15 of gestation, after irradiation at 7.37 watts of forward power (which corresponds to 123 mW/cm²) for less than 5 minutes. The predominant feature is the hematomas, both throughout the body and particularly in the brain region.

Anomalous fetuses were observed through the range of average doses used in the study. Normal litters were also observed almost throughout the same range. However, the number of litters without anomalous fetuses decreased as the average dose increased. The decrease in normal litters suggests the possibility of a dose-effect relationship. However, the available data are too limited and too divergent to establish the relationship conclusively.

Above 4.2 cal/g, exencephalies were observed as shown in Figure 8. Exencephaly

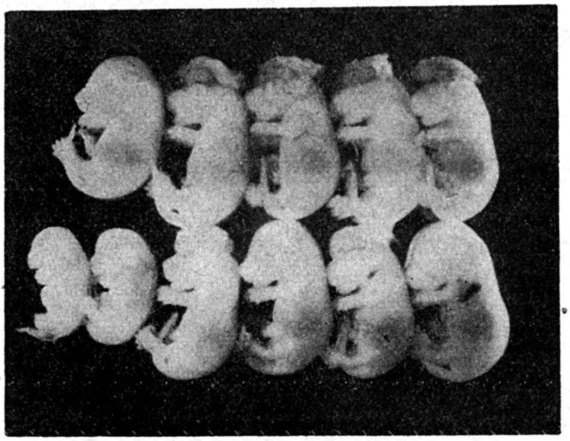


Fig. 9. One entire litter with six exencephalies and two dead fetuses (lower left), and three "apparently" normal. A variety of effects can be observed even within a single litter.

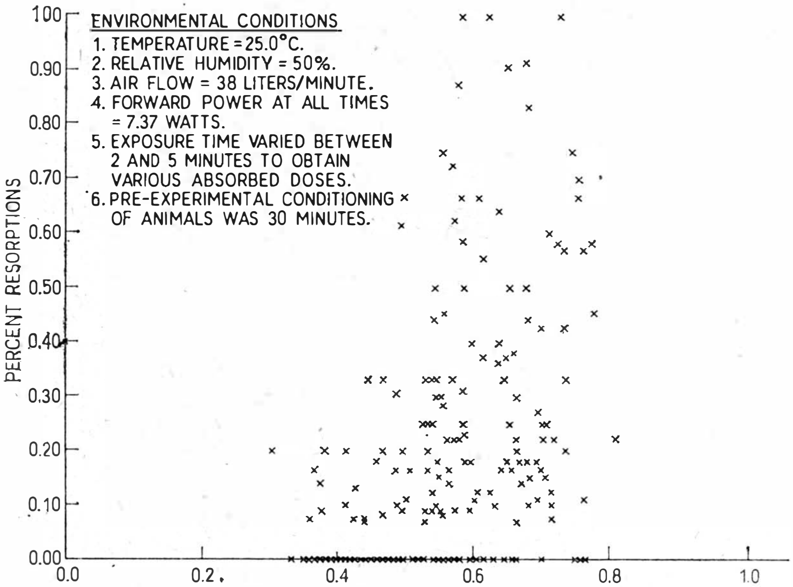


Fig. 10. Incidence of resorption observed after various average doses of microwave radiation. Each point represents the percent of resorbed embryo observed in individual litters.

is a brain hernia which is consistently caused by ionizing radiation in fetuses of the CF_1 mouse. Peak induction of exencephaly by ionizing radiation occurs at day 8 of gestation in these mice. Microwave irradiation did not produce exencephaly as frequently as does x-irradiation (6). The maximum production of the anomaly involved about 60 percent of a single litter. Exencephaly in a single litter is shown in Figure 9. At 8 cal/g of microwave radiation, the average expectancy of exencephaly was approximately 12 percent.

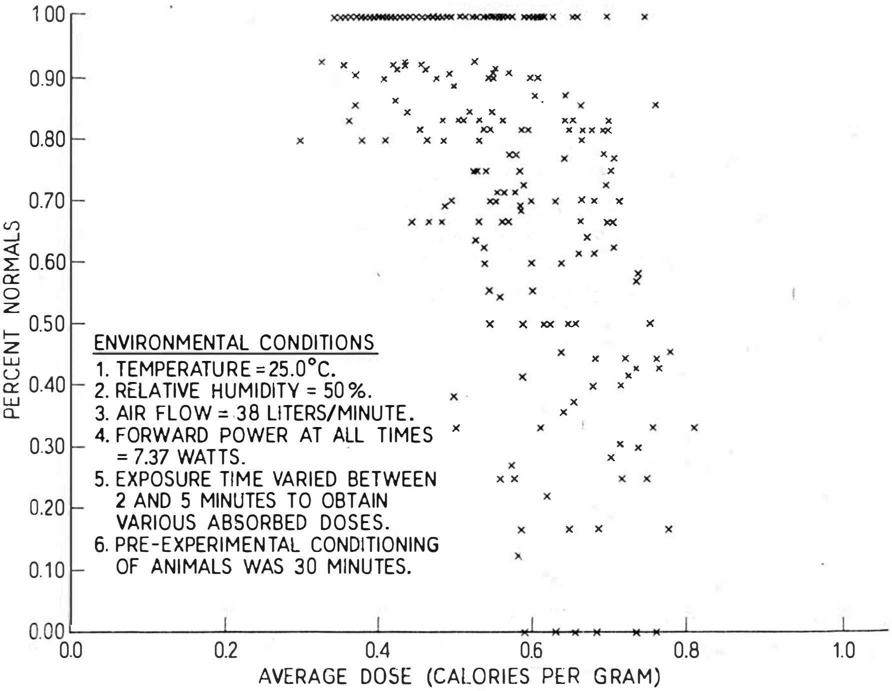


Fig. 11. Incidence of topographically normal fetuses after exposure to various absorbed doses of microwave radiation. Each point represents the percent of "apparently" normal fetuses observed in individual litters.

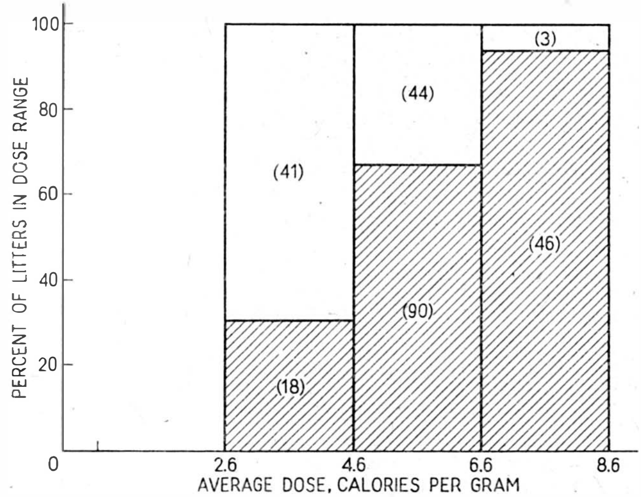


Fig. 12. Frequency of normal and anomalous litters after microwave exposure in the indicated ranges of average dose. Symbols: white columns = all litter mates normal: hatched columns = one or more resorption or anomaly. Total numbers of litters examined are shown in parenthesis.

Resorptions are evidence in the dissected uterus that development had begun. The ovum had been fertilized, implanted, and developed to some extent, but development had ceased and there remained only a partially resorbed mass resembling a blood clot. Some anomalies could be included in resorption data, since they could kill *in utero* and certainly the fact of resorption would imply an abnormal condition. Figure 10 shows a very wide distribution of incidence of resorptions, from 3.0 cal/g to 8.2 cal/g. At doses up to 7.8 cal/g, litters were observed in which there were no resorptions. However, at the higher doses the incidence of litters without resorptions is much reduced. Between 6.0 and 8.0 cal/g average dose, three litters were completely resorbed.

The calculation of normal offspring versus average dose is shown in Figure 11. It must be pointed out that normality is based upon rather gross analysis, meaning absence of any easily detectable structural anomaly. Many of the fetuses which were designated as normal could have been abnormal upon histopathological examination. Doses to pregnancies that yielded 100 percent normal offspring ranged from 3.4 cal/g to 7.8 cal/g, with decrease in frequency, while those with 100 percent abnormal offspring were observed beginning at 5.8 cal/g. Only six such pregnancies were produced up to 7.7 cal/g. As can be seen in Figure 12, the frequency of normal litters decreased as the microwave dose was increased. The concomitant increase of litters with one or more anomalous offspring, including resorptions, indicates that a linear relationship may exist between dose and fetal effects. Furthermore, there seems to be no evidence of a threshold effect. It should be pointed out that data were not obtained below doses of about 2.5—3.0 cal/g. The variation of discrete data points, such as seen in Figure 4, indicates that caution is necessary in the interpretation of the incidence of normal and abnormal litters in terms of significance and potential meaning for human health.

CONCLUSIONS AND SUMMARY

The following conclusions have been made on the basis of the study:

1. Microwave radiation can be teratogenic in mouse fetuses exposed at day 8 of gestation to average doses in the range 3—8 cal/g.
2. Gross anomalies observed in microwave-irradiated fetuses include gross hemorrhage, resorptions, exencephaly, stunting and fetal death.
3. Teratogenesis in the microwave-exposed mouse is not an all-or-none phenomenon. There is a dependency between dose and effect, without evidence of a threshold effect.
4. The distribution of microwave dose is unknown, and may account for some of the variability in incidence of fetal anomalies observed. Additional factors relating to the processes by which embryos react to microwave energy must also be taken into account.
5. The fetal anomalies reported in this paper are detectable by direct inspection. One may expect subtle and microscopically observable effects in addition to the gross anomalies.

A waveguide apparatus has been utilized so that integral dose rate to experimental animals can be determined under stable controlled environmental temperature and relative humidity. Pregnant mice were exposed within a duration of 5 minutes to a constant exposure rate of 2450 MHz radiation. Microwave-induced teratogenesis was observed among litters exposed to average doses in the range 3—8 calories per gram. Teratogenic effects observed include gross hemorrhage, exencephaly, stunting, fetal resorptions, and fetal death. Variability in the incidence of anomalies within litters indicates that the cause and effect relationships are not well enough established and understood to permit prediction of effects either in the mouse or in other species.

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Session B. Influence of Microwave Radiation on the Nervous System and Behavior

Chairman: *A. V. Roščin*
Vice-Chairman: *W. A. G. Voss*
Rapporteurs: *W. R. Adey and E. A. Lobanova*

THE USE OF CONDITIONED REFLEXES TO STUDY MICROWAVE EFFECTS ON THE CENTRAL NERVOUS SYSTEM

E. A. Lobanova

Labor Order of the Red Banner
Institute for Scientific Research on Industrial Hygiene and Occupational Diseases,
Academy of Medical Sciences of the USSR, Moscow, USSR

The harmful influence of radiowaves on the human organism, and particularly on the central nervous system (CNS), as established in the course of clinical investigations, required detailed studies under experimental conditions. Two closely related directions of experimental work were needed: a) studies aimed at defining the maximum permissible level of irradiation, and b) studies focussed on elucidation of the mechanism of action of radiowaves.

The aim of the experiments influenced the choice of method. It was deemed necessary that it should characterize the integrative activities of the CNS, possess so-called "hygienic" significance and be informative enough with regard to at least certain aspects of pathogenesis. Such a method is the use of conditioned reflexes analysis.

In this paper an attempt is made to answer the following questions:

— how do the functions of higher compartments of the CNS change following a single exposure to microwaves?

— what are the dynamics of these changes in the course of chronic irradiation?

— what are the possible mechanisms of the observed disturbances?

Before going into a presentation of our own and others authors' data, it should be noted that the most thoroughly studied are the biologic effects of microwaves, particularly in the centimeter range. By this we mean data not only on the action on the CNS, but also on effects on endocrine, circulatory, and other systems.

The functions of higher compartments of the CNS as affected by this range of wavelengths were investigated using various methods. The levels of irradiation applied by different authors varied over a broad range, but we will limit ourselves to presentation of the data obtained at intensities not higher than 10 mW/cm^2.

In hygienic investigations of this kind the method of motor-food conditioned reflexes has been used extensively. Its modification is applied successfully for producing conditioned reflexes in dogs, rabbits, rats and mice.

The preparation of the experimental animals is a very long process and consists of elicitation and strengthening of a system of positive and negative conditioned reflexes, performing a number of functional tests indispensible for defining individual peculiarities of higher nervous activities of the animals, and finally in setting up the background conditions preceding irradiation.

For characterizing the conditioned reflex activities of the animals we made use of generally employed indicators: duration of the latent period and of motor reactions in positive conditioned reflexes directed at auditory and visual analysers; the value of these parameters before and following application of the differentiating stimulus; the state of differential inhibition. The cases in which positive conditioned reflexes and natural reflexes to the sight of food had been lacking were recorded and the behavior of the animals and of functional tests were taken into account.

To facilitate analysis of the experimental material we computed these indicators and their significance for each animal and for the entire group following each series of 10 experiments during the irradiation period; this corresponded to twenty exposures to microwave radiation.

The first series of experiments was performed on rabbits irradiated during 4 months with centimeter microwaves at an intensity of 10 mW/cm^2 for 60 min daily. Following irradiation the conditioned reflexes were investigated for two months.

The conditioned motor-food reflex in rabbits was produced according to the method of O. V. Malinovsky (12); upon exposure to a sound or light stimulus the animal pulled a ring attached to a feeding trough filled with food following a conditioning signal lasting 5 s.

The action of microwaves during the first month of irradiation led to an inhibition of conditioned reflexes, as apparent from a prolongation of the latent period of the reflexes to positive signals, and, in a number of cases, even the lack of conditioned reflexes (Fig. 1). More frequently these changes were found in the first half of the stereotype, preceding application of the differentiating signal. The active inhibition, as judged by the number of disturbed differentials, was somewhat intensified.

During the second and third months of irradiation the shifts in neurodynamics were preserved. In the course of the fourth month, all indicators of the conditioned reflex activity — both fine and coarse — underwent marked changes. The conditioned reactions to positive signals appeared only after a long latent period. The ratio of the latent periods of the conditioned reflexes, after and before differentiation, increased markedly. The strength of positive conditioned reflexes following differentiation decreased, and that of the differentiation increased appreciably.

Following cessation of irradiation, normalization of the conditioned reflex activity took place only after 2 months. Hence, the inhibiting action of microwaves upon the functions of higher compartments of the CNS of rabbits under the specified conditions

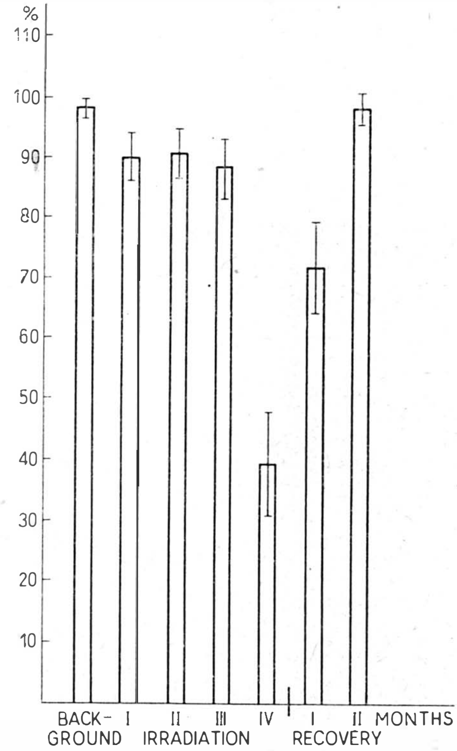

Fig. 1. Changes in strength of positive reflexes in rabbits (in percentages) and the confidence limits at 98% probability.

was apparent during the first month of irradiation and reached a maximum after 4 months.

In the second series of experiments the conditioned motor-food reflexes were established in outbred, non-stock rats by the method of L. I. Kotljarevskij (5): the conditioned animal concentrated on a feeding trough and by pushing a valve obtained its food following an appropriate stimulus of 5 s duration. Irradiation parameters for rats were the same as for rabbits.

The behavior of irradiated rats in early experiments clearly differed from that of controls. The experimental animals were less mobile and lethargic, continuously washing and licking themselves. The performance of conditioned reactions to positive signals was impeded; frequently the animals did not react to them nor, in a number of cases, even to the sight of food. Upon application of the differentiating signal the performance of conditioned reactions was improved in some experiments while in others the differentiating signal elicited an opposite effect. Finally, on occasions the animals rested immobile in the chamber, did not react to positive conditioning signals or to the sight of food and, following differentiation, fell asleep.

The described changes in the early stages of irradiation were reflected in quantitative changes in the indicators investigated and consisted of a significant increase in latent periods, frequent lack of conditioned reflexes to positive conditioning stimuli and the sight of food, the presence of phase phenomena, some deepening of differential inhibition and a resultant pronounced inhibition. It should be noted that in the course of the

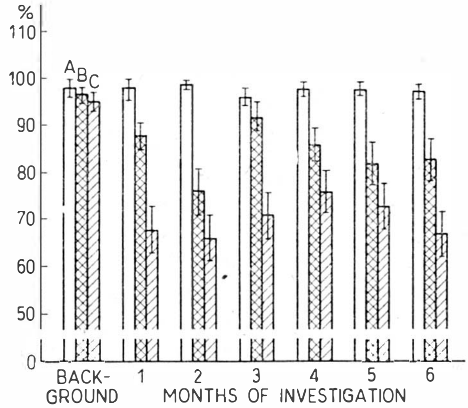

Fig. 2. Changes in strength of positive conditioned reflexes (in percentages) in control (A) and irradiated rats (inbred, B and outbred, C), and the confidence limits at 98% probability.

first month of irradiation, as compared with the following months, the changes in conditioned reflex activity were at their maximum (Fig. 2).

Upon prolongation of irradiation up to 6 months, the inhibiting influence of microwaves on the functions of higher compartments of the CNS did not change significantly except in the fourth month when they were somewhat less pronounced.

The third series of experiments was performed on K-M strain rats which, as is well known, are characterized by a higher level of excitability of the CNS and a motor reaction to strong sound stimuli; the reaction may end in convulsions.

Changes in conditioned reflexes in these rats also appeared in the course of the first month of irradiation and their character was analogous to that of outbred animals. However, the changes observed during the entire irradiation period were significantly less pronounced in outbred rats (Fig. 2).

Functional tests performed after six months of irradiation and taking the form of a strong sound stimulus and a strong inhibition of positive conditioned reflexes did not reveal significant differences in comparison with control and among the experimental groups.

It might be concluded from the data presented above that the K-M rats, that is to say, the animals with a more excitable CNS, are more resistant to the action of microwaves.

However, another trial in which the animals were starved for 24 h, revealed some differences between these two groups of animals. In outbred rats the increased excitability of the CNS due to starvation led to slight facilitation of the conditioned reflex activity, although this was not significant, while in inbred animals deterioration of the activity followed. It was less expressed in the first test after starvation, but progressed with further challenges in a way very characteristic of neurotic conditions.

In the fourth series of experiments on chronic irradiation of K-M strain rats, their reaction to an intense sound stimulus (100 dB, 90 s) was investigated systematically (once a week). During the first month of irradiation no significant changes in parameters of the motor reaction were revealed.

During the second month of irradiation, however, two out of ten rats stopped reacting to the stimulus, and in the remaining animals the period of latency of the reaction

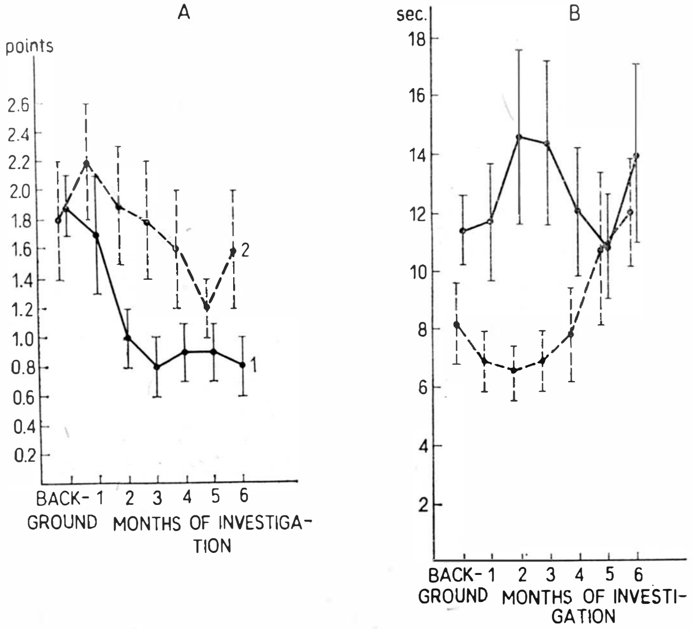

Fig. 3. Changes in the intensity of the motor reaction (A) and the latent period of the reaction in seconds (B) in irradiated (1) and control (2) K-M strain rats. Mean values and the confidence limits of the parameters at 98% probability are given.

increased significantly and the intensity of reaction, as assessed with the five-point scale of L. V. Krušinskij (8), decreased. This situation persisted during 4 months of irradiation. After 5 and 6 months, the differences between irradiated and control animals were insignificant (Fig. 3).

It follows that after microwave irradiation the excitability of the CNS, and particulary of brain formations responsible for carrying the motor reactions to sound, were lowered. However, the genetically inherited aptitude for reacting with motor excitation to an intense sound stimulus changed later and was less dependent on the influence of microwaves than the conditioned reflexes acquired during irradiation.

In the fifth series of experiments rats were irradiated with pulsed 10 cm waves of 10 and 1 mV/cm^2 intensity, the time of action being the same. Without dwelling upon details of the results obtained we will only mention that their characteristics at 10 mW/cm^2 were essentially the same as those described above and that the changes in conditioned reflex activity after 4 months of irradiation were less pronounced at 1 mW/cm^2. Application of a pharmacologic pretreatment (subcortical introduction of caffein at doses of 10, 50 and 100 mg/kg) substantially facilitated the appearance of conditioned reactions in rats irradiated with 1 mW/cm^2; in rats irradiated with 10 mW/cm^2 the high dose of caffein (100 mg/kg) elicited an opposite effect.

Conversion of the positive and negative meanings of the conditioning signals was performed by irradiated rats in the same manner as by control ones.

In the sixth series of experiments, rats were irradiated with continuous 10 centimeter waves of 10 and 1 mW/cm^2 intensity and conditioned reflexes were investigated during irradiation. Prior to irradiation the animals were distributed into three groups according to their reaction to a strong sound stimulus, with parallel controls in each group.

Irradiation lasted for 15, 30 and 60 min at a time and was applied at weekly intervals. Duration of the latent period and magnitude of the positive conditioned reflexes were investigated along with stability of the latter and the state of differentiation. The means of these indices and their confidence limits were computed, and the variance distribution of the latent periods was studied. Evaluation of differences in the distribution of a parameter between the groups of irradiated and control animals, and between those irradiated under different conditions, was carried out by means of a non-parametric criterion of A. N. Kolmogorov and N. V. Smirnov (16).

It has been found that, in comparison with controls, differences in distribution of latent periods of conditioned reflexes could not be considered as due to mere chance but are significant for 1 mW/cm², 15 and 60 min irradiations (λ = 1.82 and 2.37, resp.). In the first case an obvious displacement towards short latent periods took place; in the latter, in the direction of longer latent periods. Also significant was a difference in distribution of latent periods in animals with lowered food excitability irradiated with 1 and 10 mW/cm² for 15 min (λ = 1.37).

It follows that 10 mW/cm², 15 min irradiation does not influence significantly the level of excitability of the CNS, while 1 mW/cm², 15 min somewhat increases it.

With few exceptions, we did not succeed in finding any differences in reactions of rats to microwave irradiation dependent upon the level of food motivation and the character of reaction to sound stimuli. However, studies on the way in which the establishment of an orientation reaction to an incidental stimulus affected a conditioned reflex response made it possible to reveal changes in the CNS which were masked under ordinary experimental conditions, and the expression of which depended on the level of food motivation. In all three experimental variants (Tab. 1) the differences were significant in comparison with controls and also among the groups, and they clearly demonstrated a major bio-effect of microwaves at 10 mW/cm² intensity.

It follows that even a single short exposure to microwaves may result in CNS changes which could be disclosed by means of functional tests. The experiments on rabbits

Table 1

Influence of an orientation reaction on a conditioned reflex response (assessment of differences in distribution of latent periods of the response by means of the λ test)

Irradiation parameters	Level of food excitability		Control		Low level of food excitability			
					10 mW/cm², 15 min		10 mW/cm², 15 min	
			Background	Test	Background	Test	Background	Test
10 mW/cm², 15 min	high	background test	*0.29*	2.18	*0.45*	3.21		
10 mW/cm², 15 min	low	background test	*0.75*	2.82			*0.3*	2.13
1 mW/cm², 15 min	low	background test	*0.77*	1.49				

and rats presented above show the degree to which results of such acute experiments can be extended to conditions of chronic irradiation at 10 mW/cm² intensity. The effects of exposure at 1 mW/cm² are demonstrated in the following series of experiments, in which animals were irradiated at that intensity for 60 min daily for long periods of time.

During first exposures, behavioral changes were seen: the rats washed themselves continuously, and towards the end of the experiment they frequently fell asleep; sometimes they did not react to the sight of food, conditioned reflex responses were delayed and the differential inhibition was deepened. In the majority of rats this type of behavior continued for 18 treatments, and in some of them even longer. After 18 irradiations, as seen in the graph, the picture changed and the differences between irradiated and control

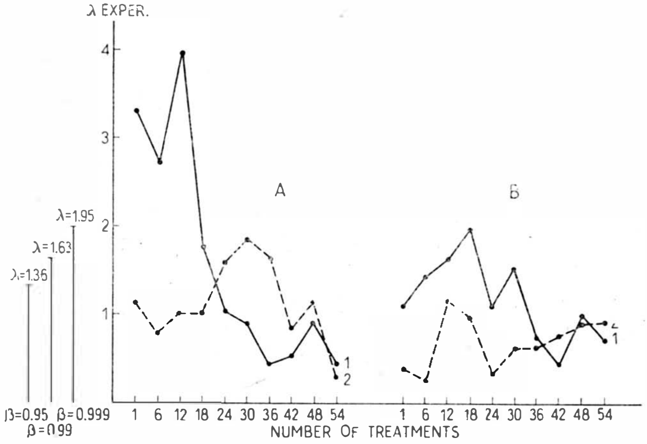

Fig. 4. Evaluation of differences in distribution of latent periods of positive conditioned reflexes (A) and time of differentiation (B) in irradiated (1) and control (2) rats as compared with the background and judged by the λ test.

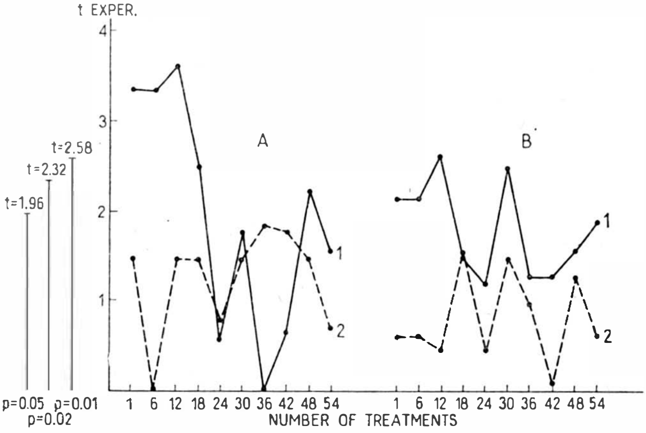

Fig. 5. Evaluation of differences in strength of a positive conditioned reflex (A) and differentiation (B) in irradiated (1) and control (2) rats as compared with the background by means of the Student-Fisher t test.

rats became insignificant (Figs. 4 and 5). Only the employment of the functional test in the form of an incidental stimulus after 48 treatments disclosed hidden disturbances of the CNS in the irradiated animals, similar to those caused by a single irradiation. The λ value of 1.37 was found upon assessment of differences in the distributions of latent periods of conditioned reflexes in irradiated versus control rats.

To sum up the data quoted above, the method of conditioned reflexes is sensitive enough; it allows demonstration of functional changes in the higher compartments of the CNS and their various patterns, which depend upon microwave intensity, duration of irradiation, its character (single, chronic), species of experimental animals, and the initial state of the CNS.

The data presented deal with conditioned motor-food reflexes. Other authors have studied salivary-nutritive, vegetative and defensive conditioned reflexes in dogs, rabbits, rats and mice exposed to centimeter wavelengths of closely similar characteristics — 10.5 and 1 mW/cm^2. Conditioned salivary-nutritive reflexes were investigated after single or repeated 2 h microwave irradiation of 5—10 mW/cm^2 intensity (17). Reactions to single irradiation were largely dependent upon the type of higher nervous activity of these animals. In animals belonging to the "strong type" (less labile) a stimulating effect was observed, while in the "weak-type" (more labile) inactivation ensued.

Analogous changes accompanied systematic daily irradiations. In "strong type" animals the conditioned reflex secretion of saliva increased in the course of the first 4—5 sessions, and henceforth gradually returned to the initial level. In "weak type" animals oscillating changes of conditioned reflexes were observed, with alternating periods of lowered conditioned reflexes, phase phenomena and so-called normalization periods.

Investigations of cardiac and respiratory conditioned reflexes in rabbits after 30 min irradiation with centimeter wavelengths at 5 mW/cm^2 intensity did not reveal any regulatory changes (23). Under the influence of a few irradiation treatments, a number of animals disclosed a lowered expression of cardiac and respiratory conditioned reflexes lasting for a few days and followed by oscillating changes in the reflexes.

A single exposure of rats to microwaves of the same characteristics was not reflected in changes in cardiac conditioned reflexes, and only a systematic irradiation of 4—5 weeks' duration led to a weakened conditioned reflex regulation of heart action (24).

In rats irradiated *in utero* with centimeter wavelengths at 10 mW/cm^2 intensity for 20 min daily during 20 consecutive days, the conditioned reflex activity was characterized by a delayed acquisition and adaptation, and also a lowered ability of preservation of a conditioned reflex for escaping from a T-shaped labyrinth with an electrified floor (15).

Investigations of conditioned reflex activity of mice in a T-shaped labyrinth showed that after 10 daily treatments the performance of the conditioned escape reflex is worsened (6).

Therefore, the investigations on conditioned reflex activity of animals with various levels of organization of their nervous system (dogs, rabbits, rats and mice), as obtained by means of different methods, showed essentially that the waves of centimeter length suppressed the functions of higher compartments of the CNS.

The conclusion that microwaves act upon the nervous system of the litter irradiated while *in utero* is important from the theoretical, and particularly practical, points of view. The supposition that changes in the functional state of the CNS of irradiated pregnant animals are the cause of disturbed functions of higher compartments of the CNS in the postnatal ontogenesis of rats seems most probable. These data indicate the need for great caution in assuming that irreversible bioeffects of microwave irradiation occur only at thermogenic levels (15).

It is obvious that the recorded changes in conditioned reflex activity of the animals are not specific for microwaves. Similar disturbances may appear as a result of the action of other exogenous (physical, chemical) and endogenous factors. However, it is necessary to consider the possibility that severe changes may occur in the function of higher compartments of the CNS, even though these may be reversible under the specified experimental conditions.

Academician P.K. Anohin showed that for true understanding of the conditioned reflex, which is a type of activity that characterizes the entire brain, an experimental analysis of all compartments of the CNS is necessary (1). This great goal of neurophysiology is being achieved by pupils and successors of I.P. Pavlov. With the help of new methodological approaches, the role of various deep brain structures in blocking conditioned reflexes and in effecting conditioned reflex activity is being elucidated.

The complexity and difficulty of interpreting changes in conditioned reflex activity of microwave-irradiated animals with respect to the possible mechanism of action on the CNS are obvious. Although the CNS attracts the close attention of, and is thoroughly investigated by, specialists of various sorts — physiologists, electrophysiologists, biochemists, morphologists — this problem is far from being solved.

Studies of electrical activity of the brain cortex of animals after single or repeated irradiations with pulsed or continuous centimeter waves show an inactivating effect of microwaves, as expressed by the occurrence of non-paroxysmal- and paroxysmal-type changes (3, 4, 20, 22). Moreover, reactions to microwaves involve various other structures of the brain: specific and nonspecific thalamus, hypothalamus, hippocampus, amygdalae, septum and reticular formation of the midbrain (11, 21). However, the most pronounced changes concern the hypothalamus and the sensorimotor cortex.

The syndrome of generalized inactivation is the most characteristic (2). The accompanying slow, high amplitude activity as registered in the cortex may be combined with convulsive discharges in the dorsal hippocampus. Recording of a large number of outbursts of spindle-shaped oscillations in the sensorimotor cortex of microwave-irradiated animals points to the possibility that, in addition to the mid-thalamus, the nucleus caudatus is involved (13, 25, 26).

The stimulus conduction along the specific afferent pathways (rabbits, 3—4 mW/cm^2), as judged by the character of primary responses, is even facilitated. Preservation of secondary responses to light impulses makes it possible to suppose that conduction along complex polysynaptic pathways passing through nonspecific medial thalamic nuclei is also facilitated (7).

Microwave irradiation (10—0.5 mW/cm^2) leads to a lowered activity of cholinesterase in the cortex, subcortical structures, cerebellum, stem and medulla oblongata of rabbits, and is sometimes accompanied by an accumulation of acetylcholine (14, 18).

Morphological investigations of the brain cortex of irradiated rats disclose reversible lesions of cortical neurons, synapses and neuroglia (9, 10, 19). By comparison with other investigated parts of the brain, the most labile cellular structures are those of the hypothalamus. Morphological examination of neurons of the supracortical and paraventricular nuclei and investigation of their neurosecretion reveal a phasic character of the lesions following chronic microwave irradiation.

From what has been said above we suppose that functional disturbances of higher compartments of the CNS accompanying microwave irradiation stem from changed cortical-subcortical relations due to a lowered tonus of the brain cortex. The latter is probably the cause of weakened corticofugal influences, as a result of which the tonus of structures responsible for the inhibiting and regulatory functions of the brain increases.

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PHARMACOLOGIC ANALYSIS OF MICROWAVE EFFECTS ON THE CENTRAL NERVOUS SYSTEM IN EXPERIMENTAL ANIMALS

S. Barański and Z. Edelwejn

Military Institute of Aviation Medicine, Warsaw, Poland

Earlier studies on the effects of microwave irradiation on animals carried out at the Military Institute of Aviation Medicine revealed that microwaves affect the activity of the central nervous system (2, 3, 4, 7, 8, 9).

The aim of this paper is to present an attempt to analyse the effects of chronic microwave exposure of experimental animals on the activity of different structures of the central nervous system.

Microwave exposure was carried out at doses below thermal levels. During these studies drugs stimulating or inhibiting the function of the central nervous system at different levels were used.

METHODS

Male, one-year old rabbits weighing about 3.0 kg were used. The animals were kept under constant environmental conditions and were all subjected previously to chronic irradiation with pulse-modulated 10 cm microwaves at a power density of 7 mW/cm^2. The total period of irradiation was approximately 200 hours (3 hours daily exposure).

Investigations were performed on two main experimental groups: The first group of 45 animals was subdivided into 3 subgroups (A, B and C), 15 rabbits each.

Animals from the subgroup A were given intravenous injections of chlorpromazine (Fenactil), 4 mg/kg of the body weight.

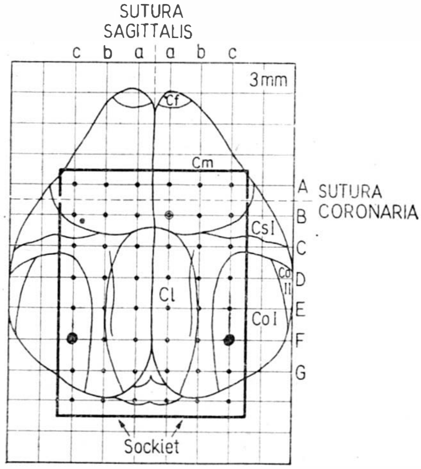
Subgroup B received intravenously a 1% solution of pentetrazole (Cardiazolum), 3 mg/kg of the body weight.

Animals from the subgroup C received intravenously an aqueous solution of phenobarbitone (Luminal), 40 mg/kg of the body weight. Unirradiated animals, receiving an identical treatment were used as controls. Subsequent experimental procedure was identical in both control and irradiated animals.

After the period of irradiation, cortical screw electrodes were implanted into the skull of all animals. Electrodes were placed symmetrically in the regions of the motor, sensory and visual cortex. Electroencephalographic recordings were made after the irradiation cycle was terminated as well as after administration of drugs.

The second experimental group consisted of 20 animals. In these animals the action of chronic irradiation on the most typical components of evoked potentials in the visual cortex was investigated. The experimental procedure was essentially the same as in the former group.

In this group 5 unirradiated rabbits served as the controls. In these animals superficial electrodes were implanted into the symmetrical points of the visual cortex, which permitted the recording of evoked visual potentials from the symmetrical points of both cerebral hemispheres.



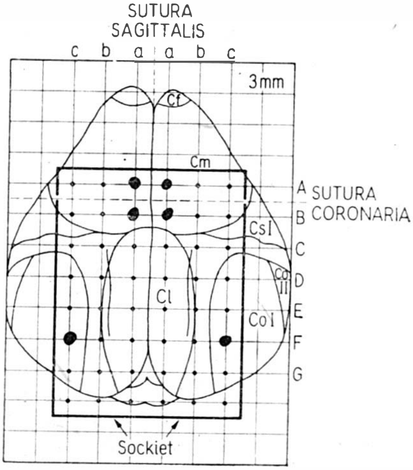


Fig. 1. The points of implantation of surface cortical electrodes.

Fig. 2. Diagram of implantation of surface cortical electrodes used during registration of evoked visual cortical potentials.

Visual potentials were evoked by the retinal stimulation with a flash of light of 700 lux intensity and 1 c/s frequency emitted by a stroboscope (Rydan). In all experiments the conditions of stimulation were kept constant.

During the experiments an "Anops" computer connected with the EEG apparatus (Elema Schönander) was employed. The analyzed period was 66 ms and comprised 128 repetitions.

RESULTS

Analysis of the electroencephalographic records shows that the effects of chronic irradiation may be detected in all of the recorded parameters. Figure 3 shows an EEG record obtained in a control animal in relaxed, wakeful stage as well as in a rabbit following chronic exposure to microwaves. In the latter case the high degree of desynchronization of the EEG pattern in all of the recorded leads was observed.

Administration of chlorpromazine (4 mg/kg i.v.) produced EEG synchronization in both irradiated and control animals.

Intravenous administration of pentetrazole (3 mg/kg) produced a long-lasting afterdischarge of rapid onset in irradiated animals, whereas in control rabbits only a series of subthreshold spindles consisting of 3—4 c/s spikes were observed.

Marked differences between the action of phenobarbitone on irradiated and control animals were noted. In rabbits exposed to chronic microwave irradiation a desynchronization of the EEG pattern was still marked after drug administration.

In a further series of experiments the effects of chronic exposure to microwaves on the main components of visual potentials were determined. Figures 7a and 7b show visual potentials in control rabbits and an animal previously exposed to microwaves. As may be seen, all the main components were markedly changed after irradiation as compared with the control response.

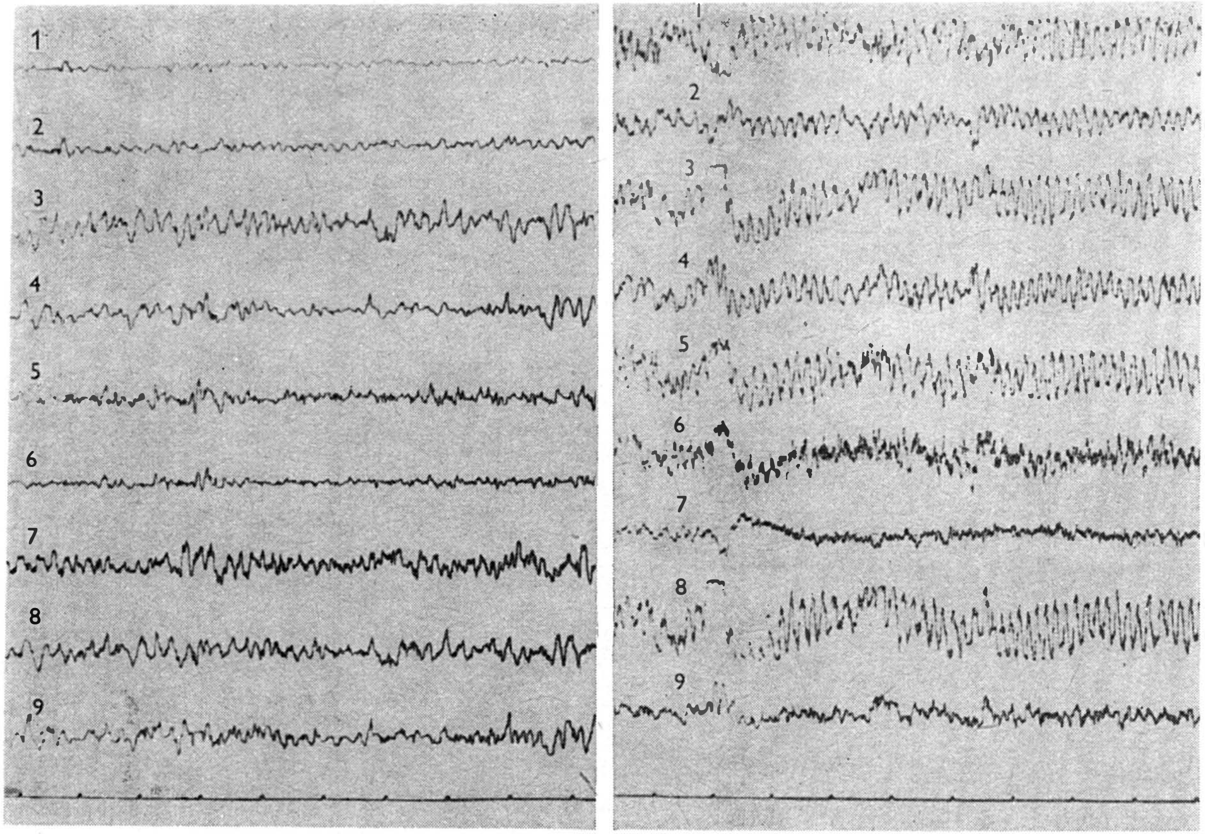


Fig. 3. Left panel: electrocorticogram in control rabbit. Right panel: electrocorticogram in animal previously irradiated. Note a desynchronization with relatively high voltage amplitude in EEG pattern. Leads: *1* — left sensorimotor, *2* — right sensorimotor, *3* — left sensorioptic, *4* — right sensorioptic, *5* — left motor-right motor, *6* — left sensory-right sensory, *7* — left optic-right optic, *8* — left motor-optic, *9* — right motor-optic.

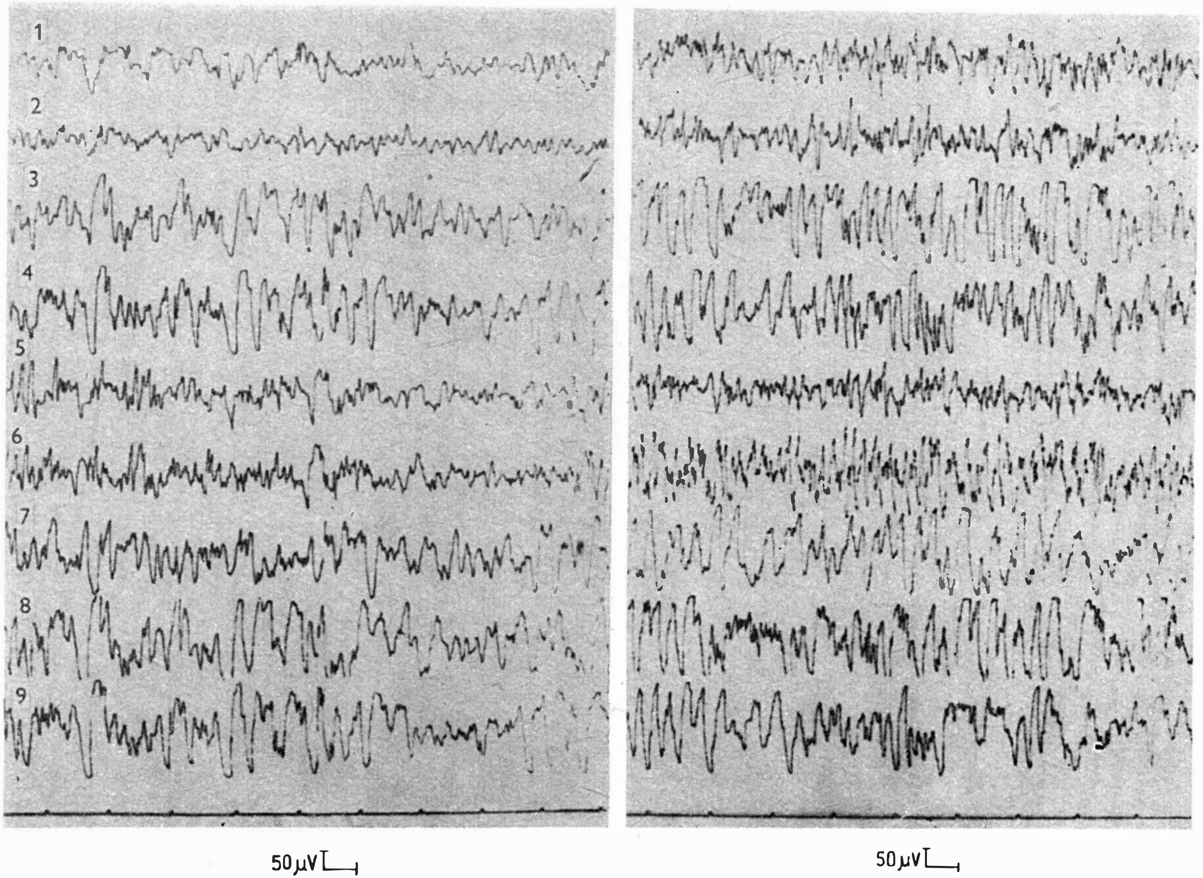


Fig. 4. On the left: effect of chlorpromazine (4 mg/kg i.v.) on the EEG pattern in control rabbit. On the right: as on the left but in animal previously irradiated. Leads: as in Fig. 3.

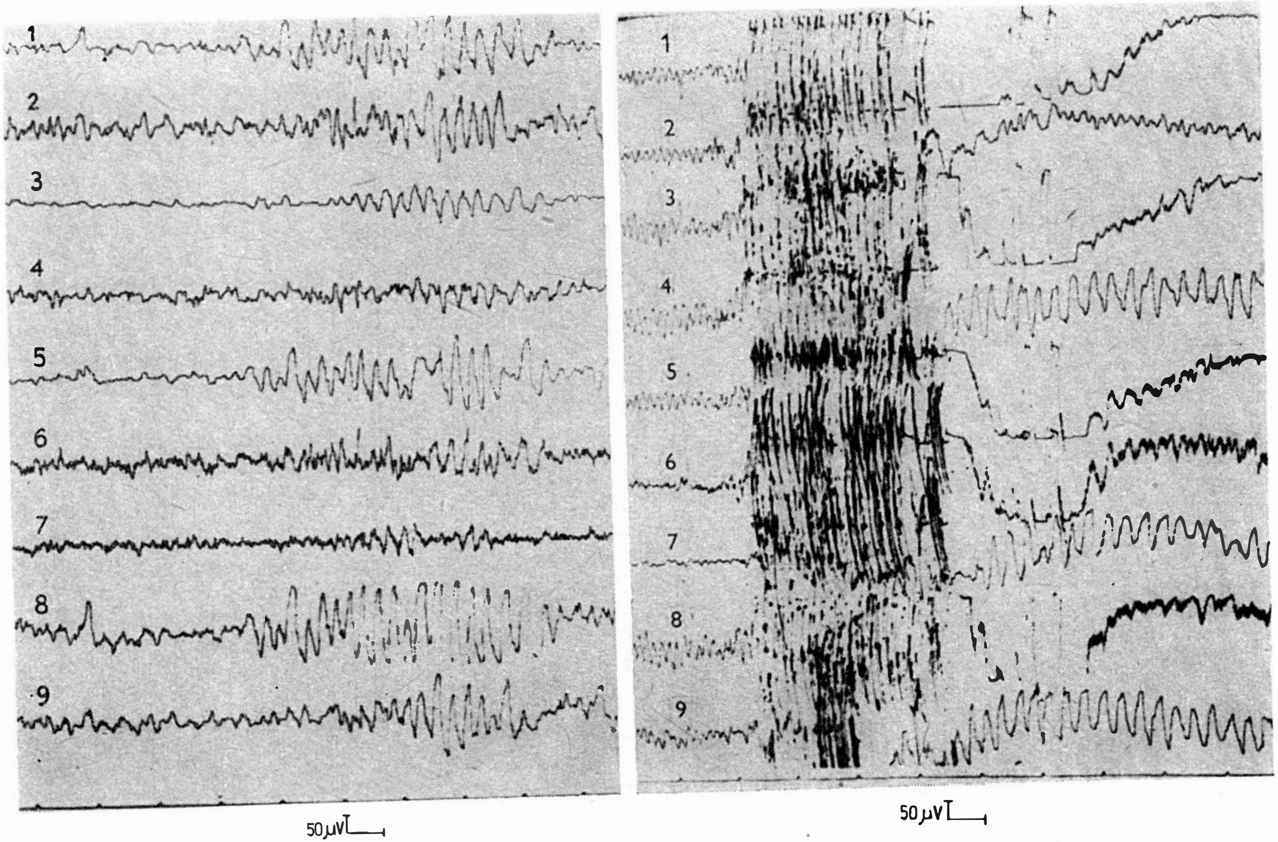


Fig. 5. Panel on the left: action of pentetrazole (3 mg/kg i.v.) on the EEG pattern in control rabbit. Panel on the right: action of pentetrazole on the EEG pattern in rabbit previously exposed to microwaves. Note the series of high-voltage spikes in all of the leads. Leads: as in Fig. 3.

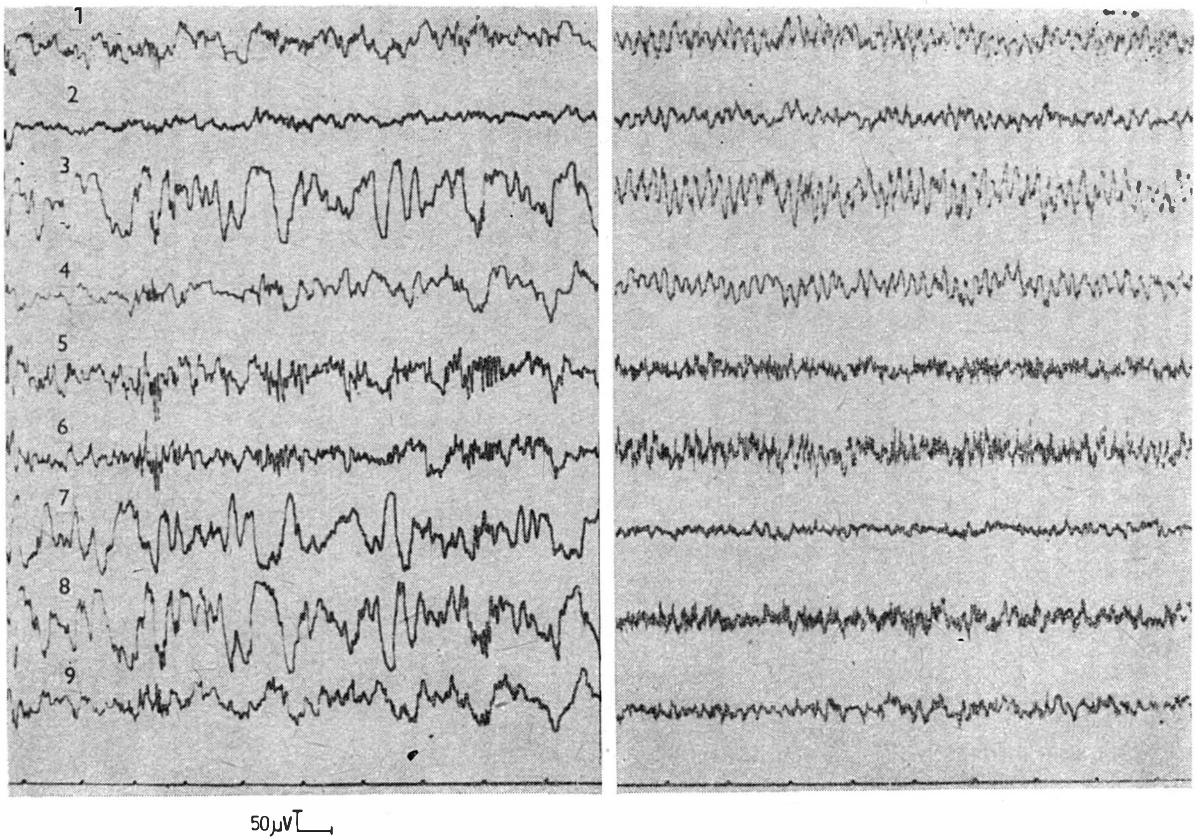


Fig. 6. On the left: effect of phenobarbitone (40 mg/kg i.v.) on the EEG pattern in control animal. On the right: same as on the left but in rabbit previously irradiated with microwaves. Note alternately occurring waves and spikes. Leads: as in Fig. 3.

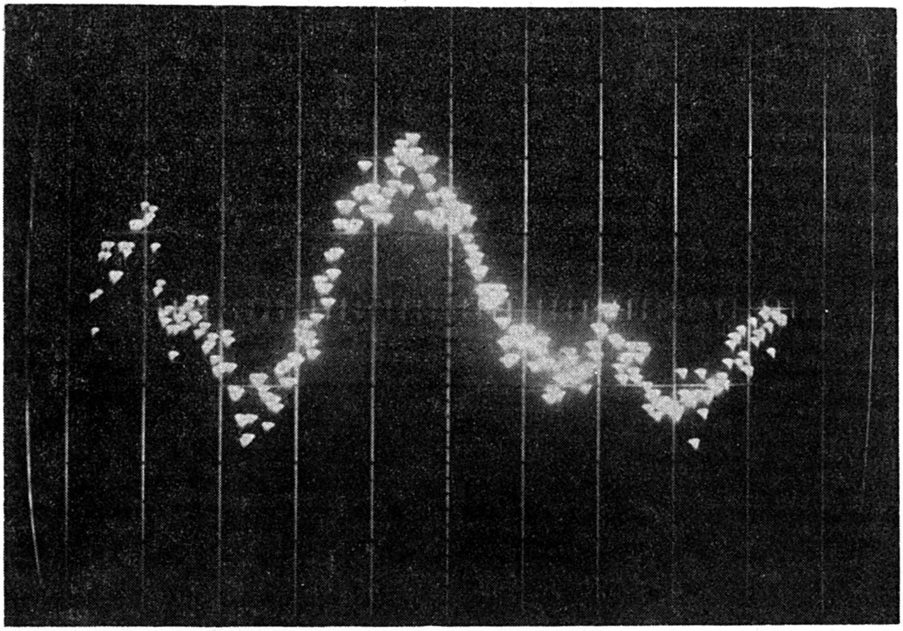


Fig. 7a. Evoked visual cortical potential in a normal rabbit.

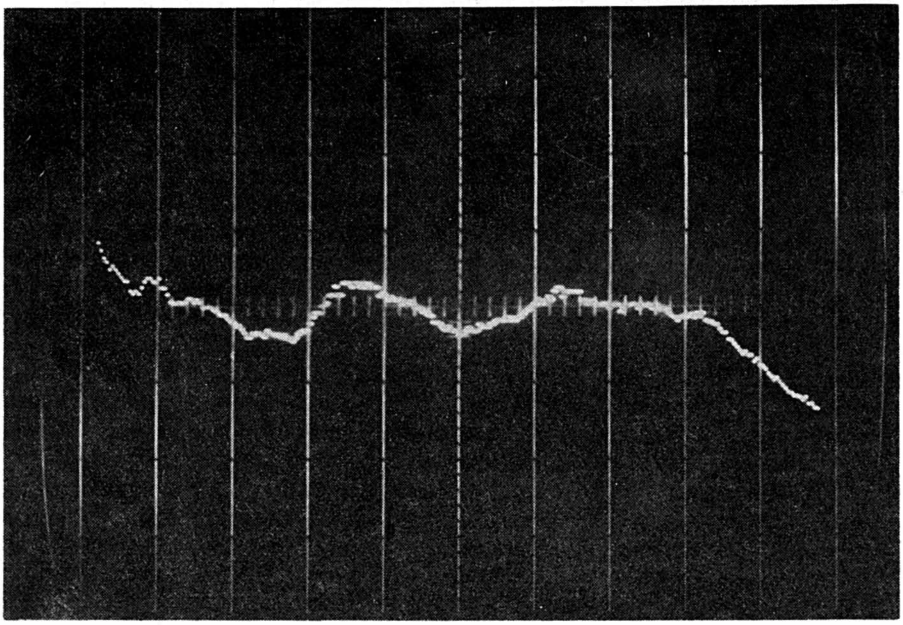


Fig. 7b. Same as in 7a but in an irradiated animal. Note the changes in all the components of the evoked visual potential.

DISCUSSION

The above-described experiments demonstrate that chronic exposure to microwaves at subthermal doses markedly changes the EEG pattern in experimental animals.

Desynchronization of the EEG pattern observed in irradiated animals is most probably due to the activation of the ascending part of the mesencephalic reticular formation (Fig. 3). Administration of chlorpromazine induced rapid synchronization of a previously desynchronized EEG pattern, which may suggest an antagonism between the action of microwaves and chlorpromazine on the structures of the central nervous system (Fig. 4). It is commonly known that chlorpromazine acts directly on the midbrain reticular formation (14, 15) and decreases its spontaneous activity (12). Essential for the central action of chlorpromazine is also the effect of this drug on the activation produced by cortical stimulation (13) as well as the influence exerted on the synaptic connections between the collaterals of the ascending lemniscal system and unspecific reticular formation (5). It may be suggested therefore that the antagonism between the effects of chlorpromazine and microwaves depends first of all on the opposite action of these factors on the activating part of the reticular formation and cerebral cortex.

In order to estimate the sensitivity of the cortical structures and reticular formation we have used a 1% solution of pentetrazole, a drug which is known to exert a facilitating action mainly on the thalamic part of the reticular formation and motor cortex (10, 11, 16, 17). The experiments described have shown that irradiated animals react more strongly than control rabbits (Fig. 5).

Similar experiments performed with phenobarbitone administration resulted in a slight facilitating action of this drug on EEG desynchronization in irradiated animals (Fig. 6).

Marked differences in the evoked visual cortical potentials were observed in irradiated rabbits as compared with control animals (Fig. 7a and 7b). As is commonly known (1) the individual components of the evoked visual potential possess different origins and their shape is determined by the temporal correlation of two afferent activating waves determining the occurrence of positive and negative phases. It may be accepted that all changes in evoked potential parameters are due — at least partially — to the functional state of afferent systems transmitting the specific and unspecific impulses.

It is of interest to note an important role of synaptic connections within the separate cortical fields, especially both facilitating and inhibitory postsynaptic influences.

Analysis of the shape of the visual cortical potential in rabbits exposed to chronic microwave irradiation demonstrated that more pronounced changes are observed in the electronegative component. This component expresses the impulses transmitted by the unspecific afferent system. The above-mentioned data confirm our previous hypothesis that the nonthermic influence of microwaves depends on the activating effect on the ascending part of the reticular formation.

The data reported in this paper are of a preliminary character only and do not make it possible to determine precisely which level of separate afferent systems is responsibile for the microwave-induced disturbances in bioelectric activity resulting in the morphological changes of the evoked visual cortical potential.

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A QUANTITATIVE ELECTROENCEPHALOGRAPHIC STUDY OF THE ACUTE EFFECTS OF X-BAND MICROWAVES IN RABBITS

L. Goldstein and Z. Sisko

Department of Psychiatry. Rutgers Medical School. Piscataway, N.J., U.S.A.

Although many studies involving the effects of microwaves on brain function in animals have been carried out, there is still no clear agreement either on the nature of the changes produced or on the power density and wavelength at which these changes occur. This may be explained by the fact that the scientists involved in such studies have used different wave bands, different power densities, and further, that their consideration of the effects has tended to be qualitative rather than quantitative.

Our studies were performed on adult male New Zealand rabbits and involved chiefly amplitude measurements of the cortical brain waves. It is well established that one can detect and characterize objectively, through such measurements, states of sedation, arousal, stimulation and hyperstimulation, since they correspond to progressive changes in the EEG from low-frequency, high-amplitude waves to high-frequency, low-amplitude waves. Behavioral observations are also involved but become secondary rather than primary for the characterization of the functional states of the brain.

The main complicating feature of these studies is that, under everyday conditions, the EEG patterns of rabbits are quite variable. The animals oscillate between sedation and arousal unpredictably. It is therefore difficult, when a change from one state to another state occurs in animals exposed to microwaves, to be confident that the shift would not have taken place spontaneously in the absence of treatment. One way to deal with this problem is to induce a sustained, stable baseline state. Since, as will be seen, exposure to continuous microwaves in the X-band (9.3 GHz) was found to produce under our particular experimental conditions stimulant effects, we have used a simple method of pretreatment with a low dose of a barbiturate to induce sustained sedation, hence a stable base state which permits more reliable detection of stimulant effects. We found in previous studies that with the low dose of the sedative used, such a state is not different from spontaneous sedation as regards liability to environmental as well as drug-induced stimulatory effects.

In order to reduce the presence of metals in the pathway of the microwaves, we used as cortical electrodes extremely thin (10/1000 inch.) Formvar-coated stainless steel wires, anchored within the cranial bone by means of nylon screws and methacrylate cement. Three such electrodes were implanted, above the right and left somatosensory cortices and within the nasal bone for the common reference electrode. The leads were soldered to a small plug cemented to the top of the skull. Following recovery from surgery, the animals were carefuly trained to sit quietly (although unrestrained) in a custom-built anechoic chamber, 60 cm wide × 60 cm high × 90 cm length, and to accept intravenous injections administered by remote control via a catheter inserted in one of the marginal ear veins before each experimental session. The chamber was provided for forced ventilation and had openings for the passage of the coaxial cable connected to the horn antenna, EEG lead wires, temperature probe, DC light, and the objective of a TV camera, used to monitor the behavior of the animals on an adjacent receiver. The head of an animal was approximately 45 cm from the horn antenna. The microwaves were generated with a Hewlett-Packard signal generator and amplified by an Alfred power amplifier.

The routine of the experimental sessions was as follows: After being introduced in the chamber and having EEG leads attached and the venous catheter inserted, the animals were left undisturbed for 5—10 min. EEG recordings were then started, first for a 10 min "baseline" period and next for a 30—60 min period following administration of Na-pentobarbital (4 mg/kg in a 0.1 ml/kg volume, intravenously).

A total of 90 experiments were run on 13 animals. Forty-five percent of the experimental sessions were run without administration of microwaves during the post-pentobarbital period. In 55% of the experiments, the microwaves were turned on 5 min after injection of the barbiturate and kept on for 5 min. Thus, for inter-session comparisons, most animals served as their own controls. The changes produced by microwaves were ascertained from the comparison of the electrical activity with and without microwave treatment, plus behavioral observations.

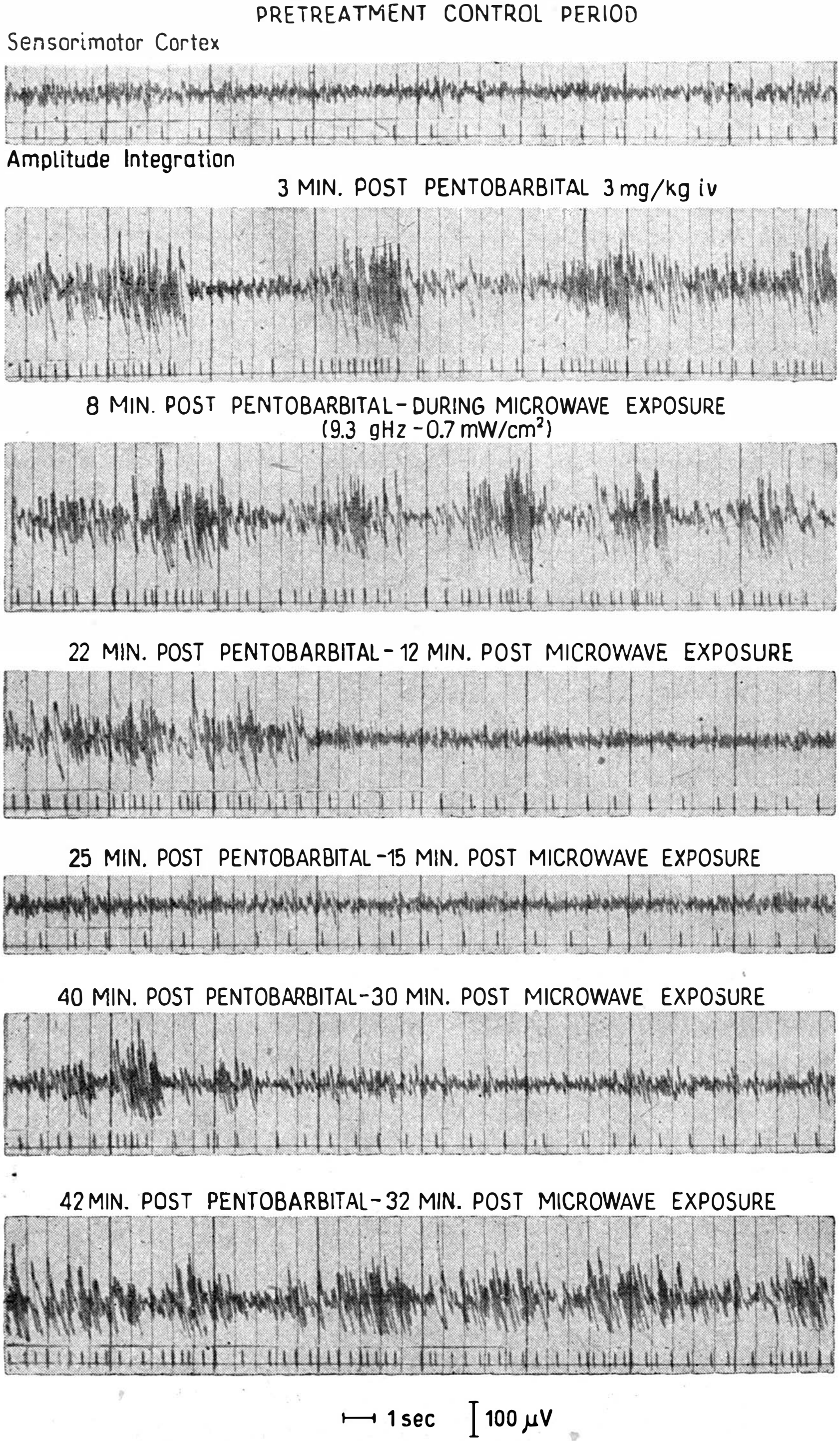
The power densities used ranged from 0.7 to 2.8 mW/cm^2. The accuracy of the dosage was verified before and after each experiment with a Narda Electromagnetic Wave Monitor. The brain electrical activity was recorded directly on paper, and, at the same time, processed through solid-state electronic integrators. These devices measure continuously on-line the amplitudes of unfiltered brain waves, and express numerically their values over time for pre-set, fixed intervals. As would be expected from the description of the EEG patterns, during sedation the integrators display much higher values than during arousal and, especially, hyper-stimulation. In this latter state, not only are the main amplitudes at a low level but also the variances of the distributions of amplitudes are small. Table 1 lists integration values for means and coefficients of variation of the amplitudes of brain waves during selected periods corresponding to the typical behavioral states previously mentioned.

Table 1

Levels of mean integrated amplitudes and coefficient of variation in rabbits during different behavioral states
(Intervals of 20 s; mean values from 12 experiments on 6 animals. N = 360)

Behavioral state	Mean EEG amplitudes	Coefficient of variation (S.D./mean × 100).
AROUSAL	35.0	23.1
Pentobarbital-induced sedation	67.8	26.2
Stimulation	27.5	18.6
Hyperstimulation	18.0	8.0

The first finding was that no detectable changes in EEG patterns, their integrated counterparts or in behavior occurred during the 5 min period of exposure to microwaves. In only 2 experiments (2%) was there a possible indication of an "on-



PRETREATMENT CONTROL PERIOD

3 MIN. POST PENTOBARBITAL 3 mg/kg iv

8 MIN. POST PENTOBARBITAL - DURING MICROWAVE EXPOSURE (9.3 gHz - 0.7 mW/cm²)

22 MIN. POST PENTOBARBITAL - 12 MIN. POST MICROWAVE EXPOSURE

25 MIN. POST PENTOBARBITAL - 15 MIN. POST MICROWAVE EXPOSURE

40 MIN. POST PENTOBARBITAL - 30 MIN. POST MICROWAVE EXPOSURE

42 MIN. POST PENTOBARBITAL - 32 MIN. POST MICROWAVE EXPOSURE

Sensorimotor Cortex
Amplitude Integration
1 sec
100 μV

Fig. 1. Direct EEG patterns and their integrated measurements in a rabbit at various stages of a microwave experiment.

effect" and an "off-effect", manifested by a brief period of sudden arousal when the microwaves were turned on and off. In all the other experiments, the state of sedation was not changed during the period of microwave administration.

The second finding was that following a latent period of 3 to 12 min there occurred a sudden arousal which lasted on the average 3 min. This was followed by a return to sedation. Again, 3 to 5 min later, a second arousal occurred, 2 to 10 min in duration. Such an alternation of periods of sedation and arousal occurred up to 4 times in certain experiments. In a number of cases, when arousal was present, it was sustained for as long as the animals were in the chamber.

Typical examples of the EEG patterns during the two phases of sedation and arousal can be seen in Figure 1. There were minimal changes during the period of microwave exposure and up to 12 min following exposure. However, at that time, there occurred a sudden arousal which lasted more than 10 min. This was followed by a return of the sedation-type activity, again followed by arousal lasting 12 min. Finally, during the last 5 min of the post-exposure period, sedation was quite prominent.

Under the direct tracings, one can see the integration pulses, the number of which is directly proportional to the cumulated amplitudes. When the successive numbers of integration pulses for fixed intervals are plotted versus time, one obtains chronograms of the electrical activity. For this particular experiment, the chronogram can be seen in Figure 2. The alternation of sedation and arousal is quite clear. It can also be seen that the variations in electrical activity during the 16 min of arousal were less pronounced than the ones present during the pretreatment control period. There was a brief arousal 6 min after microwave irradiation, but this lasted only 1 min. As a matter of fact, arousals do occur in control experiments without microwave exposure, but they are most often of short duration, at most 1 min. The power density in this particular experiment was 0.72 mW/cm^2.

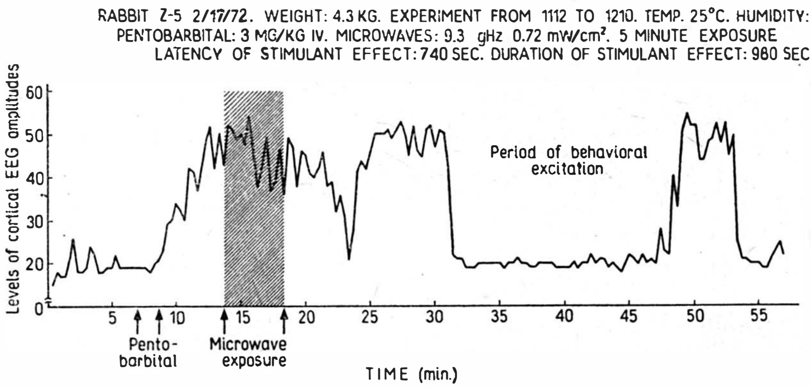


Fig. 2. Time-course changes in EEG amplitudes before, during and following microwave exposure.

In Figure 3 one can see the chronograms for another experiment with a power density of 2 mW/cm^2. The chronology of the changes is quite similar. One finds a decrease in the overall amplitudes and a 6-fold decrease in the standard deviation of the distribution of amplitudes during the period of intense behavioral excitation. The difference between the mean amplitudes during the control period and excitation period is statistically highly significant ($t = 3.1$; p smaller than 0.01). We found very similar decreases of mean amplitudes and variability in rabbits treated with hallucinogenic drugs. How-

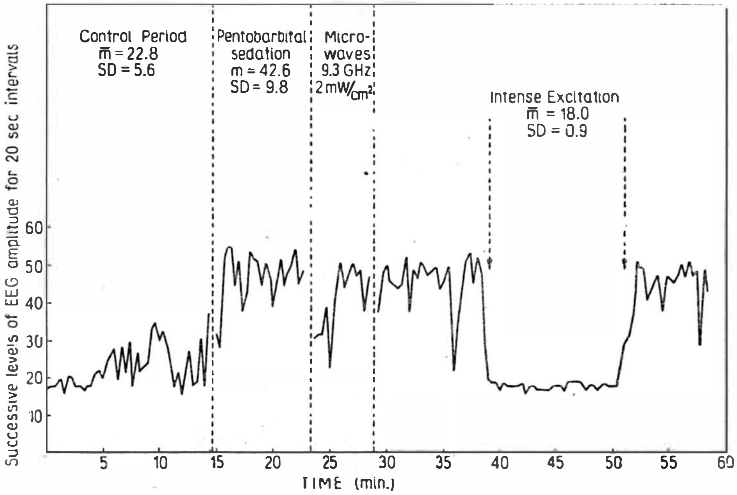


Fig. 3. Time-course changes in EEG amplitudes before, during and following microwave exposure.

ever, the difference is that with such drugs the hyperstimulation was sustained over long periods of time while with microwaves it waxed and waned.

The behavior of the animals during the periods of low EEG amplitude and variability was most unusual for rabbits, in that they exhibited repeated head movements, scratching, grooming, and uncoordinated locomotor activity. In fact, it was sometimes difficult to keep the animals in the chamber and some experiments had to be terminated early because the rabbits repeatedly unplugged the cable connecting the electrodes to the recorder by their violent jerking movements. In the example presented in Figure 3, the animal was in a catatonic-like state, with fixed gaze and a frozen posture.

Averaging the latencies for the occurrence of arousal did not reveal any significant relationship with the power density. However, the duration of arousal, computed by cumulating all the successive such periods for each experiment, indicates a possible dose-related increase. For 1.44 mW/cm^2 the duration of arousal was, on the average, of 240 ± 75 s while for 2.88 mW/cm^2, the duration was of 768 ± 78 s (nine experiments in each case; same total exposure time, namely 5 min.). In the absence of microwaves, the mean cumulated arousal time was 75 ± 12 s (12 experiments).

Although we have not been able to obtain direct measurements of the brain temperature during exposure, it seems doubtful that the EEG and behavioral effects could have resulted from a thermal change. In a number of published reports, it has been well demonstrated that with power densities of 0.7 to 2.8 mW/cm^2 there is no detectable increase in brain temperature. Furthermore, one of the most striking features of the microwave action has been the latent period following exposure, before over excitation. It is difficult to conceive of a delayed thermal effect. The same argument can be used as far as pain is concerned. If the excitatory effects result from a reaction to pain, one would have to account not only for the latency but also for the dose-related relationship. As a matter of fact, two experiments were run in which morphine sulfate (1 mg/kg) was substituted for pentobarbital: the microwave effect was as pronounced and as long lasting, with similar latent occurrence.

We do not have at present any direct indication of the mechanism (or mechanisms) of action of microwaves. However, there is a striking resemblance between the changes observed after administration of microwaves and those produced by acute injection of naturally occurring compounds modified chemically to contain stable free radicals (1). With such compounds one finds a waxing and waning of excitation-sedation periods and also a latency between administration and appearance of the effect. This raises the possibility that microwave exposure produces or enhances the formation of free radicals from naturally occurring compounds in the brain. It is interesting that the effects of free radical compounds are present in spite of adrenergic blockade, depletion of catecholamines and serotonin, as well as cholinergic blockade (2), which suggests a mechanism different from the one existing under "classical" stimulatory actions.

In the course of the experiments reported, it was found that the microwave effects disappeared when the relative humidity reached or exceeded 40%. It may be that transmission of the waves through the fur is impaired in rabbits whose long hairs are known to adsorb water. Further experimentation is planned in which this environmental factor will be controlled.

Acknowledgments

This research was carried under contracts from the U. S. Naval Air Development Center, Warminster, Pa. U.S.A.

The important contributions of B. D. Polis, Ph. D., K. D. Straub, M. D., and of Ronald Zerofsky, M. D., are gratefully acknowledged.

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PSYCHOGENIC STRESSORS ARE POTENT MEDIATORS OF THE THERMAL RESPONSE TO MICROWAVE IRRADIATION

D. R. Justesen, D. M. Levinson and L. R. Justesen

Laboratories of Experimental Neuropsychology, Veterans Administration Hospital,
Kansas City, Missouri, U.S.A.

The data of several recent studies have confirmed observations of antiquity (3) that emotional arousal in mammals is paralleled by a rise of temperature in the core of the body. An elevation of colonic temperature to one degree Celsius or more appears to be an invariant reaction of the conscious animal to physically noxious stimuli (5), to physically benign stimuli that are novel to the organism (1, 2), or physically benign stimuli which have repeatedly been associated with a noxious event (4). The elevation of temperature appears within a few seconds and, if the evoking stimulus is of brief duration, usually dissipates within one to two minutes of time. We have given the label of Evoked Thermocolonic Response (ET_cR) to the reaction and are currently using it as an index of the ability of small mammals to detect microwave energy at low rms-densities.

Because the ET_cR is a new concept from the standpoints of application, instrumentation, and measurement, some justification and qualification of its use are in order. By way of justification, we note, first, that the behavioral indicant of choice for determining perceptual sensitivity to exotic stimuli — the mix of methodologies from Pavlovian and Instrumental conditioning known as conditioned suppression — is extraordinarily laborious and time-consuming when large numbers of experimental subjects are to be studied. Second, the neurophysiological indicant of choice for scaling perceptual or emotional arousal, the electroencephalogram (EEG), has received an unfriendly welcome (and probably undeservedly so) to the radiobiological laboratory. However the possibility of passive and active interactions of microwave fields with the conductive leads that contact the skull or brain of an irradiated subject makes for a problem that is both persistent and real when animals are irradiated in the multi-mode cavity. The ET_cR, in contrast, is easily and quickly obtained. It makes use of a small, indwelling heat-sensor which can be isolated electrically from the animal, thus precluding stimulation of tissues by demodulated energy. The possibility of passive interactions still exists from injection of trapped energy into sensor-amplifying circuitry, but spurious readings of temperature can be avoided because the ET_cR is of sufficient duration that it can be observed well after irradiation of an experimental subject is terminated.

We shall qualify the ET_cR in terms of pertinent thermal characteristics of the species — the rat — to which we have given the most attention. The requisite background of parametric data is given in the first of two original experiments to be reported here; the other experiment involved comparison of ET_cR's as evoked by peripheral sensory stimulation and by microwave irradiation. In both experiments we utilized female albino rats of Sprague-Dawley lineage. The rat was selected for its economy, mass, and geometry; the female, because she lacks the elaborate arteriovenous shunt which serves as a thermoregulator in the male's testicular apparatus. The proximity of the apparatus to the large colon in the male could confound measurement of an ET_cR.

Experiment 1

Aims: 1) to determine the norm, range, and variability of the rat's nocturnally and acutely measured colonic temperature; 2) to determine whether averaged temperatures differ between animals which are manually handled only and those which are also concomitantly subjected to thermal measurement; and 3) to determine the rate at which a handling-evoked ET_cR is habituated during a series of handling treatments.

Procedure. Eighty rats which individually weighed between 250 and 300 g were obtained in a common shipment on 11 March from a local supplier. They were placed four to a cage (24 by 18 by 13 cm) in a windowless vivarium in which ambient temperatures and relative humidities were maintained, respectively, between 22 and 26°C, and 55 and 65%. While in their cages, the rats had unrestricted access to Purina Lab Chow and water. An automatically timed, 24-hour cycle of darkness and fluorescent illumination was maintained in the vivarium, the darkness occurring from 19 : 00 to 3 : 00 hours. Except for a daily change to a clean cage, for daily replenishment of food and water, and for punch-coding of the ears on 13 July, none of the rats was physically contacted by human beings until 20 July. After random division into two numerically equal groups, all 80 rats were individually handled by one of us (D.M.L.) for 45 to 50 seconds each day for six consecutive days. Handling was carried out between 7 : 30 and 9 : 00 hours during the rats' nocturnal period when they would normally be awake and active. Temperatures were measured each day in experimental animals but only during the first and sixth days in controls. It was necessary to illuminate the vivarium during the periods of handling so that the animals and recording apparatus could be visualized. Thermal measurement was made by picking up an animal in a gloved hand with the major axis of the animal's body held in a vertical position; a lubricated thermistor-probe (United Systems Model 406), which was held in the other hand, was then inserted past the animal's anal sphincter into the colon to a minimum depth of 6 cm. Each animal was held in the same, stationary position whether or not measurement of temperature was made. Stabilized readings of temperature after 30 seconds of insertion of the probe were independently read by the handler and by another investigator from the digital display of a precision electronic thermometer (United Systems Model 1502). After mutual concurrence about the reading had been reached, the second investigator recorded the values in a log book. One experimental animal and two controls had presented symptoms of pulmonary disease by the sixth day of treatment; although their temperatures were close to normal, their data were excluded from the analyses that followed.

Results and comment. Colonic temperatures of the 77 rats were persistently variable (Fig. 1), showing a range of more than 1.5°C on each occasion of measurement. The decline in averaged temperatures between the first and sixth days was smaller in experimental rats (0.74°C) than in controls (0.92°C), but not reliably so ($p > .05$), which confirmed our subjective impressions that the naive rat's distress upon being handled is not noticeably augmented by the concomitant probing of its anus and colon. The declines *per se* were highly reliable for both groups of rats (both $p \ll .01$). The large daily inter-individual differences of temperature notwithstanding, the high reliability of the declines indicates a marked degree of intra-individual stability of temperature in the downward trend across time.

A major implication of the data is that even the minimal and benign handling that was necessary to obtain an acute measurement of colonic temperature resulted during the initial treatment in an ET_cR of an averaged magnitude + 0.83°C — as extrapolated from the averaged 6-day decrements of both groups. While habituation of

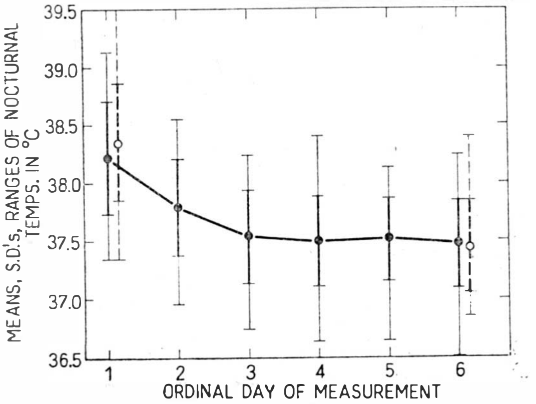

Fig. 1. Means (circles), plus-and-minus standard deviations (heavy vertical lines), and ranges (lighter vertical lines) of nocturnally measured colonic temperatures of 39 experimental (closed circles) and 38 control rats (open circles). Experimental and control rats were briefly handled each day for six consecutive days. Rats of the experimental group were concomitantly measured for temperature during all six days, control rats, on the first and sixth days only. Temperatures were measured when the rats were 4.5 to 6 hours into the 16-hour "dark" phase of an artificial 24-hour dark-light cycle. Ambient temperature at the center of the room where the rats were housed was 23.14±0.86°C during the periods when temperatures were measured.

the ET_cR to handling was rapid, occurring within the first three handling treatments in experimental animals, we discovered subsequently that the extinguished ET_cR is readily disinhibited. One week after the sixth handling treatment, the same 77 rats were wheeled in their cages from the vivarium to an adjacent laboratory approximately 45 meters away, but in the same building. Even though temperatures were measured as before and by the same handler, they averaged slightly more than 39°C. If one takes 37.5°C as the habituated nocturnal norm of our rats, it would appear that the novel complex of vestibular, visual, and acoustic stimuli that were occasioned by the move resulted in an ET_cR whose magnitude exceeded 1.5°C.

Experiment 2

Aims: In an earlier study (6), we had observed that a moderately thermalizing but non-lethal dose of microwave energy and a potent but non-lethal stressor (bodily restraint) were sometimes lethal for the rat when applied in combination. The results of the earlier study and of Experiment 1 led us to question whether smaller doses of microwave energy and a mildly aversive stimulus (faradic electrical stimulation of the feet) would: 1) evoke comparable ET_cR's; and 2) be additive when combined with respect to magnitude of the ET_cR.

Procedure. Forty-five experimentally naive rats, which averaged 303 g at the time of experimentation, were obtained from the local supplier and were housed in the vivarium, four to a cage. While in their cages the rats had continuous access to food and water. Each rat was handled for a minimum of 60 seconds by an ungloved investigator for a total of eight times during a period of four weeks. During the next four weeks, the rats were moved to the adjacent laboratory on three different occasions where they were again handled and then concomitantly measured for temperature while they were allowed to explore within a multi-mode cavity (6) which was being operated on a "standby" basis (without injection of microwave energy into the cavity). The temperature was measured by a carefully calibrated thermistor which had been encased (except for its epoxy-covered extremity) along with its tightly twisted conductive leads within a 1-meter length of flexible polyethylene tubing (outside diameter: 2.4 mm). The thermistor-and-tubing assembly was inserted through a small hole in the grille of the door of the cavity; with the door unlatched, the thermistor was then inserted into the colon of an animal to a minimum depth of 6-cm. The thermistor was held in place by fastening the tubing to the tail of an animal by a small strip of paper masking tape. When the door to the cavity was latched, the animal within could be visualized through the grille. All of the animals during the period of habituation to the inert cavity and the subsequent period of experimentation were closely observed (while light tension was maintained on the tubing) to prevent them from chewing at the tube and interfering with thermal measurement. Within the cavity was a Plexiglas chamber (inside dimensions: 37 by 24 by 25 cm) with a floor-grid which was used to supply the faradic stimulation to the feet (7). Fresh air at 22 to 23°C and 50 to 60% relative humidity was continuously circulated through the chamber with an estimated flow-rate of 2.8 cubic meters per minute.

The nominal frequency of the magnetron-generated microwave energy that was injected into the cavity by a waveguide was 2.45 GHz. The energy was modulated as a half-wave sinusoid; pulses of approximately 8 ms each recurred at 60 Hz and were mechanically mixed by a four-bladed modal stirrer that rotated between the waveguide opening and the Plexiglas chamber at 3 Hz. Dosing estimates of absorbed energy, which was calorimetrically determined (6, 8), are given in this paper as averaged (rms) values, but maximum peak values as determined from oscillographic tracings of probe-detected demodulated energy were 20 times greater.

The 45 rats were randomly assorted in equal numbers of five each into the nine possible conditions that resulted from the factorial combination of three levels of microwave dosing with three levels of intensity of faradic foot shock. The three levels of microwave dosing, stated as total-energy doses in millijoules per gram (mJ/g) were 0, 360 ±18, and 1800 ±90 mJ/g. The three rms intensities of faradic current were measured at 0, 50, and 60 μA-rms with respective maximum peak-to-peak intensities of 0, 450, and 700 μA. The faradic current was of a "grey-noise" character with a dominant frequency near 1-kHz and negligible energy above 5-kHz. Each rat received a succession of three challenges, each of which included a 60-s period of sham or actual irradiation which overlapped a $^1/_2$-s period of sham or actual faradic stimulation. The latter period commenced 50 seconds after onset of the former. An aperiodic, 30- to 180-s interval occurred between challenges. The stabilized basal temperature of each rat was measured and recorded before challenges were begun and then the peak of temperature during the 30-s period that followed each period of challenge was observed and recorded.

The "lower" and "higher" (as opposed to zero-level) dosing values of microwave irradiation were based upon dose-rates of 2 and 10 milliwatts per gram (mW/g). The two dose-rates respectively correspond to threshold and highly salient energy levels when microwave energy is used as a sensory cue by rats in our cavity-system in measures of conditional suppression (7, 9). The "lower" and "higher" intensities of faradic current were based upon subjective reactions by us when the shock was administered for $^1/_2$-s through the finger tips; the lower intensity was just above the absolute threshold for sensation while the higher, in spite of its modest increment of energy over the lower intensity, was decidedly "unpleasant."

Results and comment. Each of the three ET_cR's of each rat was calculated by subtracting the animal's basal temperature from its post-challenge peaks of temperature. For all except the rats of the control condition (zero radiation, zero foot shock), there was a virtually linear incrementing of magnitudes of the successive ET_cR's — each challenge was followed with few exceptions by an additional increase of peak-temperature. To simplify the presentation of the data, we report the averaged magnitude of the ET_cR which occurred after the third (and final) challenge (Fig. 2). A factorial analysis of variance revealed that irradiation and foot shock, as independent sources of variation, were highly reliable triggers of the ET_cR (both F-ratios >8.5 at 2 and 36 d. f.; both $p \leq .01$). The interaction of irradiation and foot shock was nil (F-ratio = 1.13 at 4 and 36 d. f.; $p > .05$), indicating that the two classes of "stimuli" in combination neither masked nor synergized but were simply additive with respect to controlling the magnitude of the ET_cR.

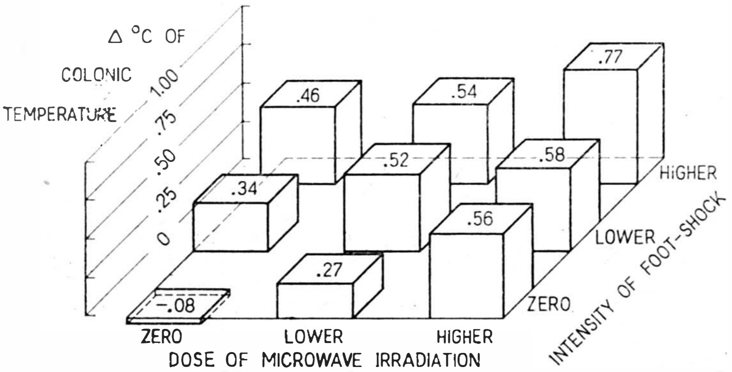

Fig. 2. Averaged elevations of colonic temperature over baseline values of nine groups of female rats which had been thrice exposed within a 7-min period for 60-s to 2.45 GHz microwave irradiation (0, 2, or 10 mW/g) and for 0.5-s to faradic foot shock (0, 50, or 60 μA-rms) in a factorially designed experiment. Anesthetized controls (data not shown) exhibited a maximum averaged elevation of +0.06 °C.

For purposes of providing additional control data another factorially controlled study was performed. Four additional groups of five rats each, all with a pre-experimental history comparable to that of the animals of Experiment 2 were given the sham and "higher" treatments of irradiation and foot shock. The treatment conditions replicated those of Experiment 2, except that the "lower" level of irradiation and of foot shock was omitted. Thirty minutes prior to the first challenge, each rat was dosed with a hypnotic, sodium pentobarbital (intraperitoneally: 35 mg/kg). None of the averaged ET_cR's of the four groups exceeded +0.06°C, a finding which supports our contention that the occurrence of an ET_cR is a cognitively mediated event. Without perception of a (potentially threatening or alien) stimulus, there will not occur that quickening of nervous activity that somehow leads to a rise of core-temperature.

Discussion. Our findings confirm and extend those of Livšic (10), who demonstrated that the cord-transected or sympathectomized mammal exhibits much less of a rise in body temperature than does the intact animal when each is illuminated by the same density of EM energy. We are not certain of the meaning of Livšic speculation that

"...direct action of UHF energy upon the higher nervous centers..." is implicated by his findings. If he means a specific effect not explicable in terms of thermalization of tissues, we would take a conservative and contrary view at the present time. We argue on grounds of parsimony for an explanation based upon non-specific (thermal) stimulation. Perhaps a faint sensation occurs in the irradiated animal that is attributive to or derivative from a slight or uneven warming of innervated tissues. If so, minuscule amounts of energy could be translated into a potent psychogenic stressor. The stressor could be, that is, a signal of peripheral origin that only secondarily stirs the central nervous system to increased activity and has the tertiary consequence of evoking the transient hyperthermia that we call the ET_cR.

There is a widespread assumption, even among many biological scientists, that the body temperature of the mammal is largely invariant. While small variations are recognized as a normal accompaniment of circadian and ultradian rhythms, and larger variations, the result of pathological conditions, relatively little attention has been given to the factors of individual differences and cognitive interactions. The data of Experiment 1 revealed that mammalian body temperatures — at least those of rats — are quite variable from animal to animal, even in a controlled environment. The data of Experiments 1 and 2 also revealed that body temperature is reliably elevated by seemingly physically benign events — by handling, by change of surroundings, by tactile stimulation, by a weak faradic current, and by irradiation by low average densities of microwave energy. The finding that the combined application of microwave irradiation and novel tactile stimulation is additive with respect to the magnitude of the ET_cR should be a caveat to the radiobiologist. While he is grappling with problems of physical artifact, he must come to understand that they are compounded by those of psychogenic origin. The antidote for both problems is rigorous, well conceived, and well controlled experimentation in which monitoring of temperatures of intact animal subjects is no longer a nicety but an imperative.

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Our work was supported by 8200 Research Funds from the U. S. Veterans Administration, by Contract Funds (DADA 17-68-C-8021) from the Surgeon General, U. S. Army, and by Grant from the U. S. Public Health Service (1-RO1-RL000678-01). We thank M. Barsky, R. Clarke, R. Halsey, R. Cohn, and M. Gardner for assistance and Profs. Edward Wike, Charles Sheridan, and Roland Fischer for advice and criticism.

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SOME EFFECTS OF VARIOUS PULSED FIELDS ON ANIMALS WITH AUDIOGENIC EPILEPSY

I. Štverak, K. Marha and G. Pafkova

Institute of Aviation Medicine, Prague. Czechoslovakia
Institute of Hygiene and Epidemiology, Prague, Czechoslovakia

The problem of biological effects of pulsed modulated waves has not been dealt with consistently in the literature. It is not clear, for example, what is the significance of rapidly occuring, short-lasting, but pronounced changes in the momentary high peak value of the proper SHF-carrier wave. In other words, the question arises, to what extent the carrier modulation contributes to greater biological effectiveness of pulsed fields.

We attempted to solve the problem by comparing the effects of electrostatic pulsed fields, microwave pulsed fields and continuous fields. Changes in rats and mice with an inherited predisposition to epileptic seizures after sound stimulation (bell) were investigated in chronic experiments. In the first series the animals were exposed to a pulsed electrostatic field.

The present communication presents results of the second series of experiments in which animals were submitted to the action of a pulsed electromagnetic field. The amplitude of the electric component of the field corresponded to the experimental conditions in the first series.

METHODS

Experiments were performed on 40 rats reacting with epileptic seizures to a sound stimulus. 24 animals were irradiated and 16 served as controls. Starting with the second day after birth, the rats were submitted for 4 h to the action of a pulsed electromagnetic field daily for 10 weeks excluding Saturdays and Sundays.

The rats were placed in the field of electromagnetic radiation in perforated Perspex boxes. The position of individual rats during consecutive exposures was changed stepwise in such manner as to irradiate the animals evenly.

During irradiation the temperature was recorded continuously in two fixed boxes.

Weighing of the animals was done weekly starting with the 4th postnatal week. Testing by means of a bell was performed also from the 4th week of life onwards once a week, 6 times altogether. If after 60 s of uninterrupted ringing there was no change in behavior, for this particular examination the reaction of the rat was considered as "zero".

In animals which reacted to sound stimulation with motor reaction which ended, as a rule, in convulsions, the interval between the initiation of ringing and the onset of seizures was recorded. Neither the duration of seizures nor the length of the recovery phase was assessed.

We manipulated the control group similarly, including transfer to experimental premises but without irradiation.

The generator of pulsed electromagnetic radiation emitted waves at 2850 MHz frequency. Pulse duration was 2.7 μsec and repetition frequency 357 Hz. The average power density within the area of exposure amounted to 30 mW/cm^2.

A constant temperature of approximately 23°C was maintained in the animal house. During experiments, i.e. from 8 a.m. till 12 noon, the temperature in the experimental room increased from 23°C to 26°C, while that in the Perspex boxes varied from 24.7°C to 27.8°C.

During the experiments we paid attention to changes in body weight, the interval from sound signal to the onset of the seizure, and the percentage of null reactions in irradiated and control animals. In addition we recorded the number of animals which died. Results are expressed in percentages and evaluated by means of the t-test.

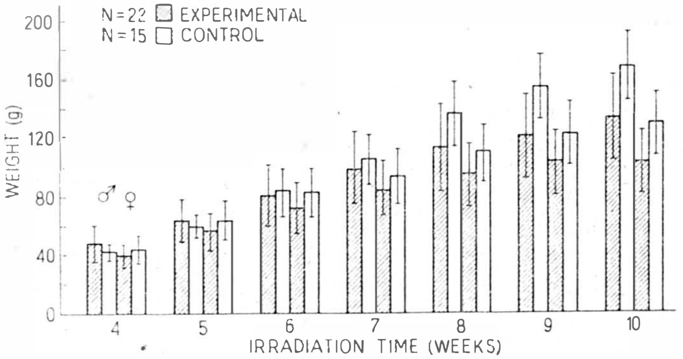

Fig. 1. For explanation, see text.

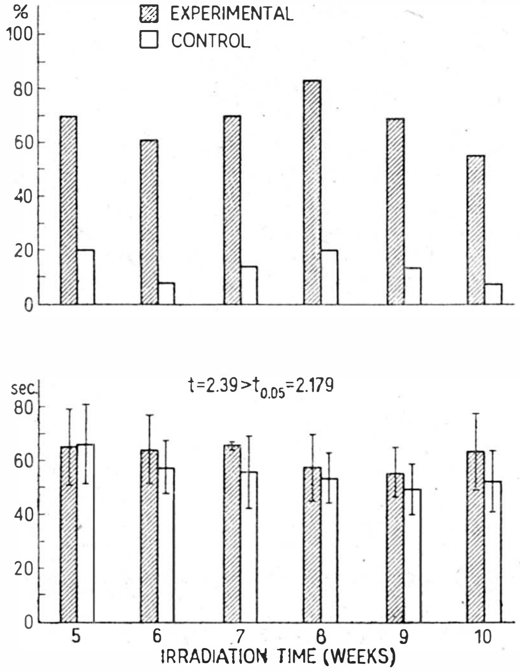

Fig. 2. For explanation, see text.

RESULTS

Figure 1 shows changes in weight of irradiated animals of both sexes and of controls. From the 4th to the 10th week of life the body weight tended to increase in all animals, more in males than in females. The body weight of irradiated animals was insignificantly lower than that of controls.

The upper half of Figure 2 illustrates the occurrence of null reactions in rats. The hatched columns represent the frequency of such reactions in irradiated animals, and the plain ones their frequency in control rats.

The null reaction occurred in approximately 70% of animals in the irradiated group and in 20% of the controls (percentages relate to the number of animals in separate groups).

The bottom section of the graph compares mean intervals between the start of ringing and the onset of seizures in irradiated and control animals. The hatched columns relate to irradiated animals and the plain ones to controls. In all cases the mean time preceding the onset of seizures is longer in irradiated than in control animals. The results obtained during the sixth week of experimental observations were significantly different at the 5% level; the remaining differences were statistically insignificant.

One control and 2 irradiated rats died during the first 4 weeks. No further deaths occurred during the remaining six weeks of irradiation and tests.

DISCUSSION

The results presented above form part of a long-term, multi-stage study aimed at characterization of pulsed fields of various types by means of investigating responses of the nervous system of rats with audiogenic epilepsy to sound irritation. The separate stages involve irradiation with a pulsed electrostatic field, a pulsed electromagnetic field and a continuous field.

Results obtained with a pulsed electrostatic field (pulse duration, 10 μsec; amplitude, 800 V; repetition rate, 769.2 Hz; field gradient, approximately 130 V/cm) (4) showed that irradiation of rats with audiogenic epilepsy (starting with the 4th day after birth, 4 h daily for 10 weeks) led to prolongation of the interval from the beginning of sound stimulation to the onset of seizures. In addition, a higher number of null reactions expressed in percentages occurred in irradiated animals.

In both cases results of 10 weeks' irradiation show a tendency to lowered sensitivity to sound stimulation of audiogenic rats and more frequent occurrence of null reactions.

It has been known from the literature that Soviet authors have investigated exposure of rats with audiogenic epilepsy submitted to a pulsed electromagnetic field (1, 2, 3). They obtained similar results although their methods differed. Also different was the mean power density (10 mW/cm^2).

In conclusion it could be noted that a pulsed electrostatic field and a pulsed electromagnetic field within the microwave range, when applied to rats sensitive to sound signals in methodologically identical experiments, resulted in lowered sensitivity and a significantly increased number of null reactions. In this stage of experiments the results show a possibility that modulation influences the biologic effects of pulsed electromagnetic fields.

We plan to examine the effects of a continuous microwave field by means of the same methods in the next stage of this long-term experiment. Then, detailed analysis of all results obtained so far will be conducted.

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INTERACTION OF ELECTROMAGNETIC FIELDS AND LIVING SYSTEMS

C. Romero-Sierra, J. A. Tanner and J. Bigu del Blanco

Department of Anatomy, Queen's University, Kingston and Control Systems Laboratory,
National Research Council, Ottawa, Canada

INTRODUCTION

There is an increasing need to master one of the most basic life processes, namely the interaction of electromagnetic fields from within and without tissue. This interaction occurs at all levels of complexity from the cell to the organism and plays a vital role in the maintenance of life itself.

The authors have been working for more than a decade on the basic phenomena underlying electromagnetic interaction. This report presents a review of their work together with a conceptual viewpoint of the emerging laws that govern such interactions.

EXPERIMENTAL FINDINGS ON INTERACTION EFFECTS

The findings obtained earlier were published as indicated in the reference list. To avoid repetitions only the general topics which were the subject of these investigations, will be indicated. Escape reactions of birds (42, 43), patterns of escape behavior (44), changes in egg of chickens in a very-low intensity microwave field (29), changes in EEG and EMG patterns in domestic fowl (30, 48), feathers as sensory detectors of microwave fields (45), and the interaction of these fields with feathers (4—7, 31), interaction of microwave fields with parakeets in flight (32) and the effect on feeding behavior of Leghorn hens (46) were studied. Gross effects on plants were also examined (33, 46).

Another series of experiments concerned effects on peripheral nerves of rats (13, 22, 24, 34—36), acceleration of the process of wound healing (14, 15, 17, 19, 23, 37) and changes in the diffusion rate of aqueous solutions of electrolytes through membranes (8, 9) as well as effects on the rate of flow and mass flux of liquids flowing along tubes of small diameter (10).

BIOLOGIC CONSIDERATIONS OF MICROWAVE RADIATION*

Extensive but inconclusive and controversial studies have been conducted in this area. An excellent source of references up to 1965 is Pressman. Since then, many other publications on this subject have appeared including our own contributions.

The interaction of microwaves with living systems is a subject of extreme complexity,

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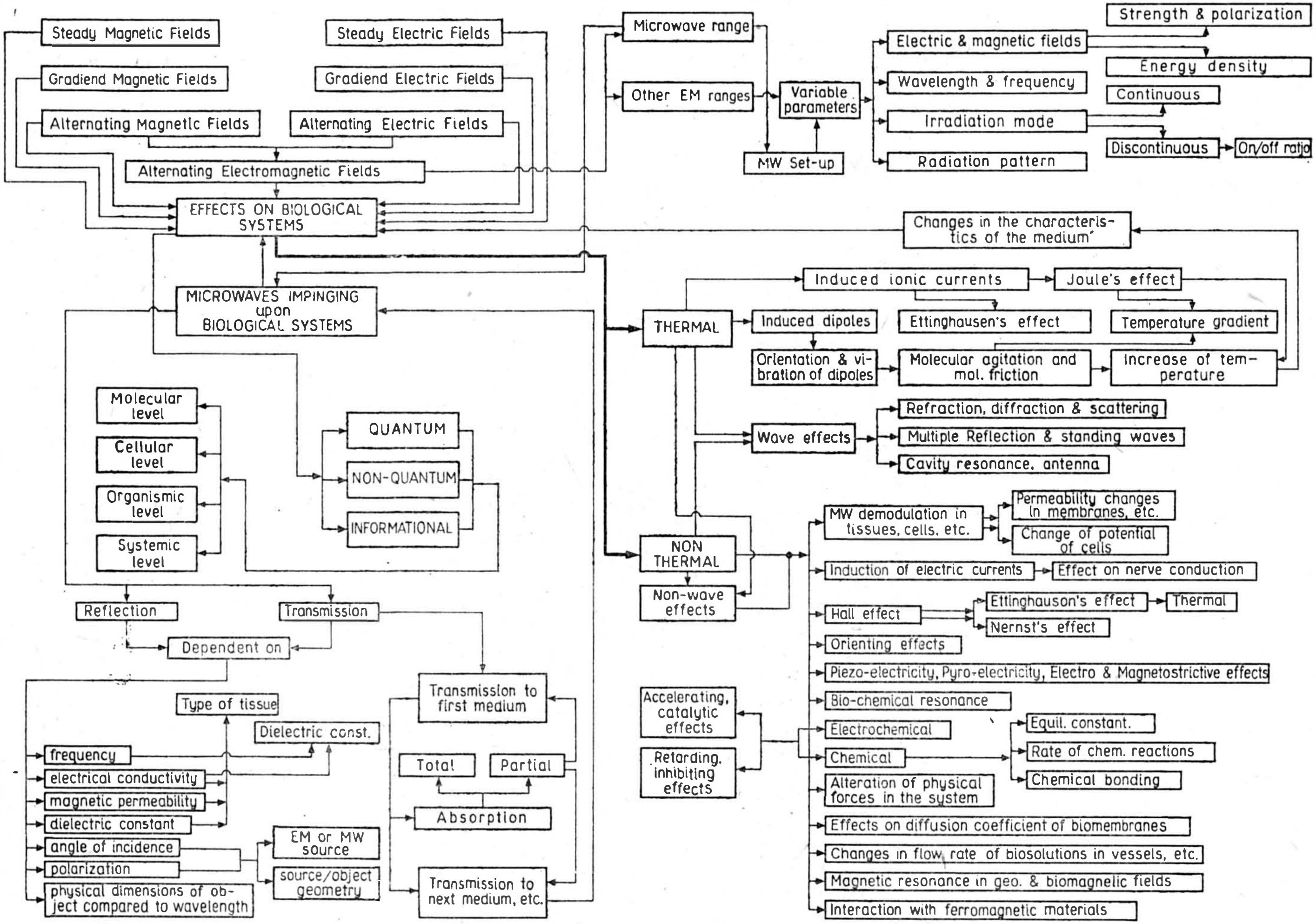
* References: 1, 2, 11, 12, 16, 18, 20, 21, 24, 25, 26, 27, 28, 38, 40, 41, 47.


Steady Magnetic Fields
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Steady Electric Fields
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Alternating Electric Fields
Alternating Electromagnetic Fields
EFFECTS ON BIOLOGICAL SYSTEMS
MICROWAVES IMPINGING upon BIOLOGICAL SYSTEMS
Microwave range
Other EM ranges
Variable parameters
MW Set-up
Electric & magnetic fields
Wavelength & frequency
Irradiation mode
Radiation pattern
Strength & polarization
Energy density
Continuous
Discontinuous
On/off ratio
Changes in the characteristics of the medium'
THERMAL
Induced ionic currents
Joule's effect
Induced dipoles
Ettinghausen's effect
Temperature gradient
Orientation & vibration of dipoles
Molecular agitation and mol. friction
Increase of temperature
Wave effects
Refraction, diffraction & scattering
Multiple Reflection & standing waves
Cavity resonance, antenna
NON THERMAL
Non-wave effects
MW demodulation in tissues, cells, etc.
Permeability changes in membranes, etc.
Change of potential of cells
Induction of electric currents
Effect on nerve conduction
Hall effect
Ettinghauson's effect
Thermal
Nernst's effect
Orienting effects
Piezo-electricity, Pyro-electricity, Electro & Magnetostrictive effects
Bio-chemical resonance
Electrochemical
Chemical
Equil. constant.
Rate of chem. reactions
Chemical bonding
Alteration of physical forces in the system
Effects on diffusion coefficient of biomembranes
Changes in flow rate of biosolutions in vessels, etc.
Magnetic resonance in geo. & biomagnelic fields
Interaction with ferromagnetic materials
Accelerating, catalytic effects
Retarding, inhibiting effects
Molecular level
Cellular level
Organismic level
Systemic level
QUANTUM
NON-QUANTUM
INFORMATIONAL
Reflection
Transmission
Dependent on
Type of tissue
Dielectric const.
frequency
electrical conductivity
magnetic permeability
dielectric constant
angle of incidence
polarization
physical dimensions of object compared to wavelength
EM or MW source
source/object geometry
Transmission to first medium
Total
Partial
Absorption
Transmission to next medium, etc.

Fig. 1. Interaction of MW fields with biosystems.

as depicted by the block diagram of Figure 1. In this diagram an arbitrary division has been made between wave and non-wave effects in order to point out some of the wave effects common to all electromagnetic radiation. Some of these interactions can be correlated with the biological effects elicited. However, a considerable amount of work has yet to be done in this field to elucidate the subtleties that would lead to an understanding of the observed effects at very low intensity radiation levels.

Biological effects can be divided into three categories (see Tab 1):

Table 1

Microwave field intensity ranges corresponding to the identifiable biological effects

Non-thermal	1 μW—100 μW
Thermal, non-heating	100 μW— 10 mW
Heating	10 mW and above

1. Heating effects.
2. Thermal, non-heating effects.
3. Non-thermal effects.

This division requires some clarification. Thermal, non-heating effects are effects identified with changes in temperature and heat balance not attributable to the direct conversion of MW energy to heat in tissue. Numbers are allocated to the intensity levels in Table 1 but it should be borne in mind that these are subject to gross variation when individual differences between living systems are taken into account. The same applies when the host of environmental parameters that profoundly influence the biological effects of microwave radiation are taken into account.

Irradiation intensities below 100 $\mu W/cm^2$ are considered non-thermal for both pulsed and CW beams, either with general or local irradiation of humans and animals. At a power level of 10 mW/cm^2, the energy transformed into heat in the body is roughly equal to the heat loss per square centimeter of body surface of humans and warm-blooded animals under normal environmental conditions. On this basis power levels between 100 μW and 10 mW are non-heating although thermal mechanisms may be involved.

The interaction between EM fields and living systems is dependent on three groups of factors:

Group A — Characteristics of the radiation.
Group B — Characteristics of the environment.
Group C — Characteristics of the biological receptors.

In essence, (i) all these factors must be thoroughly understood and measured if one is to predict the effect of any kind of non-ionizing electromagnetic radiation and (ii) it is important to note that there is interplay between the groups of factors. This interplay is depicted in Figure 2 as the intersection of the sides of a triangle representing the three groups of factors. A sample set of parameters is tabulated in Table 2.

Because of the dramatic effects produced by thermal MW levels resulting in permanent damage and/or death of the biological specimen under irradiation, the short-term thermal level combination has been the most fruitful area of experimentation. Little work has been done on the short-term, non-thermal and long-term, non-thermal modes of MW radiation.

Since it is reasonably easy to detect and monitor high radiation levels we emphasize the importance of the last two irradiation modes. From these we consider the long-term

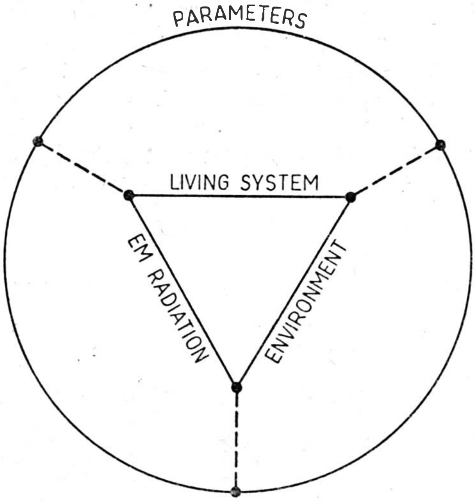

Fig. 2. Schematic presentation of the interaction of living systems with EM radiation and the environment.

Table 2

Sample table of parameters

Living system	EM Radiation	Environment
Type	Duration	Temperature
Species	(Long-term, short-term)	Pressure
Age	Frequency	Humidity
Sex	Power flux density	Atmospheric composition
Metabolic state	Modulation	Light intensity
Stress	Far field	Particulate matter
etc.	Near field	Air velocity
	etc.	EM radiation (natural sources)
		Sound level
		Vibration
		etc.

non-thermal combination as being of the utmost importance because of the present-day proliferation of MW systems.

MECHANISM OF INTERACTION

The interaction of electromagnetic fields with living systems is a highly complex subject and can be viewed in the light of the many mechanisms potentially involved — see Figure 1.

Because heat is usually involved in the interaction of a MW field with the biosample, effects were originally observed at MW levels that produced a measurable increase in the temperature of the specimens. Tissue and biological fluids being lossy materials of relative high electrical conductivity, high ohmic losses occur in them which are proportional to E^2. Thus the effect of an electric field (or its magnitude squared) has predominance over the magnetic field.

In the region where the predominant effect is heating of tissue it is obvious that the electric field plays a key role. In this region subtle non-thermal effects may be obscured. The question arises as to what happens in the non-thermal region. How are the electric and magnetic fields related to a specific non-thermal effect and what interaction takes place on a molecular or macroscopic level? It is important to note that very little attention has been given as yet to the effect that the magnetic field associated with the MW may have on a biological system.

In the light of the strong EM interaction between glial and neuronal cells and in the light of the pattern of interaction between EM fields and the organism, the emerging laws of interaction appear to be as follows:

1. Electromagnetic fields imposed on a living system modify the electromagnetic interaction that exists between glial and neuronal cells inside a nervous structure.
2. To predict the consequences of any interaction, all the parameters that characterize, (i) the electromagnetic field, (ii) the environment and (iii) the subject radiated, must be quantified and integrated.
3. Electromagnetic fields interact with living systems triggering a set of interactive biophysical phenomena.
4. The unstable sequence of events triggered by electromagnetic fields impinging on living systems may be stabilized at the level of the cell, tissue, organ or organism affected.

NAVIGATIONAL ORIENTATION IN BIRD MIGRATION

Since feathers have been shown to occupy a sensory role, functioning as receiving antenna arrays in electromagnetic fields, it follows that birds could conceivably use their feathers to obtain directional information. Migratory birds are affected by temperature and humidity to the point of triggering the migratory process. It is known that these two parameters modulate the sensitivity of feathers as antennas. Therefore it may be hypothesised that synchronization of the two corresponding biological processes provides the stimulus to the animal to seek a particular flight path in its continuing search for an optimal equilibrium.

Supporting evidence exists in the well-known phenomenon of disorientation and confusion that occurs with birds held captive for a short time during migration. A period of captivity introduces a discontinuity in the birds' spatial and temporal perception of the minute gradients in temperature, humidity and electromagnetic field. During this period changes occur in these parameters and when the birds are released they are confronted with a new environmental pattern and a new set of gradients from which to derive directional information. The inevitable result is disorientation.

This same concept can be applied to other migratory species. In the case of fish, for example, the appropriate biological receptors would be the scales.

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Session C. Effects of Microwave Radiation at the Cellular and Molecular Level

Chairman: *E. H. Grant*
Vice-Chairman: *B. Servantie*
Rapporteurs: *K. H. Illinger and S. Szmigielski*

PRINCIPLES OF INTERACTION OF MICROWAVE FIELDS AT THE CELLULAR AND MOLECULAR LEVEL*

H. P. Schwan

Department of Bioengineering, University of Pennsylvania, Philadelphia, Pennsylvania U.S.A.; Max Planck Institute of Biophysics, Frankfurt am Main, Federal Republic of Germany

The electrical properties of tissues and other biological systems do not only control the mode of propagation of electromagnetic energy in tissues. They also tell us how electromagnetic fields interact with biological systems at various levels of complexity. I shall first briefly summarize the rather advanced state of our present knowledge of such properties. Next I shall draw some conclusions about possible mechanisms which may or may not cause subtle non-thermal effects. No consideration will be given to magnetic properties since the latter are, for our purposes, identical to those of free space.

ELECTRIC PROPERTIES

The first figure indicates the dielectric behavior of practically all tissues. Three relaxation regions α, β, γ of the dielectric constant exist at low, medium and very high frequencies. The mechanisms responsible for these regions are indicated in Table 1.

Inhomogeneous structure is responsible for the β-dispersion, i.e., the polarization resulting from the charging interfaces, i.e., membranes through intra- and extracellular fluids (Maxwell-Wagner effect).

Rotation of molecules having a permanent dipole moment, such as water and proteins, is responsible for the γ-dispersion (water) and a small addition to the tail of

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* This work was supported by NIH Grant HE-01253 and ONR Contract N00014-67-A-0216-0015.

Table 1

Electric relaxation mechanism

Inhomogeneous Structure (Maxwell-Wagner)	β
Permanent Dipole Rotation (Debye)	γ, β tail
Counter-Ion Relaxation Electrophoretic Relaxation	α

the β-dispersion resulting from a corresponding β_1-dispersion of proteins. The tissue proteins only slightly elevate the high frequency tail of the tissue's β dispersion since the addition of the β_1-effect caused by tissue proteins is small as compared to the Maxwell-Wagner effect and since it occurs at somewhat higher frequencies. Another contribution to the β-dispersion is caused by smaller subcellular structures, such as mitochondria, cell nuclei and other subcellular organelles. Since these structures are smaller in size than the surrounding cell, their relaxation frequency is higher, but their total dielectric increment is smaller. They therefore contribute another addition to the tail of the β-dispersion (β_1).

The γ-dispersion is solely due to water and its relaxational behavior at about 20 GHz. A minor additional relaxation (δ) between β and γ-dispersion is caused in part by rotation of amino acids, partial rotation of charged side groups of proteins and the relaxation of protein-bound water which occurs somewhere between 300 and 2000 MHz.

The α-dispersion is presently least clarified. Intracellular structures such as the tubular apparatus in muscle cells, which connect with the outer cell membranes could be responsible in all tissues which contain such cell structures. Relaxation of counter ions about the charged cellular surface is another mechanism suggested by us. Last but not least, relaxational behavior such as reported recently for the giant squid axon membrane can account for it. The relative contribution of the various mechanisms varies no doubt from one case to another and needs further elaboration.

Electrophoretic relaxation is the counterpart of the relaxation due to counter ion movement. It results from the oscillatory movement of charged particles with the alternating field. Its magnitude can be calculated and is sufficiently small to noticeably contribute to the other relaxation mechanism indicated in Table 1.

Gross structure

α — Excited membrane?
Intracellular structure?
β — Tissue structure (Maxwell-Wagner)
γ — Water

Fine strucutre

α_1 — Charge transfer (ion relaxation)
β_1 — Subcellular components, biologic macromolecules)
δ — Bound H_2O, side chain rotation, amino acids

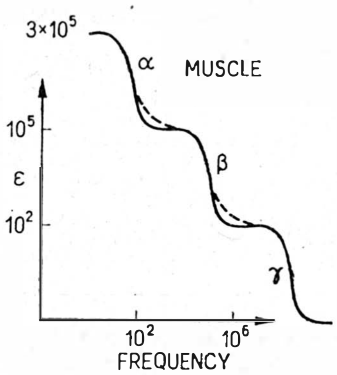

Fig. 1. Gross and fine structural relaxation contributions to the dielectric constant of muscle tissue. Dashed lines indicate fine structural contributions. The data and various structural contributions are typical for all tissues of high water content.

No attempt is made to summarize conductivity data. Conductivity increases similarly in several major steps symmetrical to the changes of the dielectric constant. These changes are in accord with the theoretical demand that the ratio of capacitance and conductance changes for each relaxation mechanism is given by its time constant or, in the case of distribution of time constants, by an appropriate average constant.

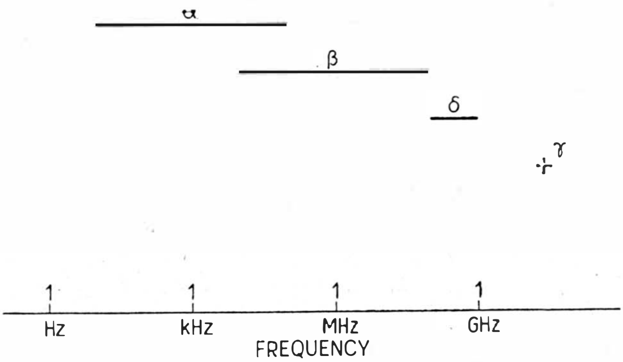

Fig. 2. Ranges of characteristic frequencies for various biological systems.

Figure 2 indicates the variability of the characteristic frequencies for the various mechanisms α, β, γ, and δ from one biological object to another. For example blood cells display a weak α-dispersion centered at about 2 kHz, while muscle displays a very strong one near 0.1 kHz. The β-dispersion of blood is near 3 MHz, that of muscle tissue near 0.1 MHz. Clearly there is considerable variation depending on cellular size and other factors. However the γ-dispersion is always sharply defined at the same frequency range and there may not be as strong a variation in the δ-effect as there is for the α- and β-dispersion frequencies.

Table 2

Dispersion characteristics of certain biologic materials

Electrolytes	γ
Biologic Macromolecules:	
Amino Acids	δ + γ
Proteins	β + δ + γ
Nucleic Acids	α + β + δ + γ
Cells, free of protein:	β + γ
Charged	α + β + γ
Excited membranes	α + β + γ

Table 2 attempts to summarize at what level of biological complexity the various mechanisms occur. Electrolytes display only the γ-dispersion characteristic of water. Biological macromolecules in water add to the water's γ-dispersion the δ-dispersion caused by bound water and rotating side groups. And proteins and nucleic acids in particular add further dispersions in the β and γ-range as indicated. Suspensions of cells free of protein would display a Maxwell-Wagner β-dispersion and the γ one of water. If they contain protein an additional comparatively weak β-dispersion due to the polarity of protein is added and a δ-dispersion. If the cells carry a net charge an α-mechanism due to counter ion relaxation is added and if their membranes on their own relax, as some excitable membranes do, an additional α-mechanism appears.

SOME CONCLUSIONS

Obviously much is known about mechanisms responsible for the electric properties of biologic materials. In all cases where mathematical tools can be applied to fairly simple shapes, as in the case of spherical cells and even erythrocytes, the theoretic prediction is precisely in agreement with the experimental data.

In cases where the complexity of biologic structure exceeds mathematical power, at least semiquantitative agreement with approximating theories has been achieved. In any case, our present understanding is sufficient to warrant confidence in the various models chosen. This is by no means meant to imply that there are no more unresolved problems. As a matter of fact the following Table 3 attempts to summarize some of the work which has to be done in the future:

Table 3

Unresolved problems

Origin of δ-dispersion
Extendend theory of counter ion relaxation and applications to macromolecules and cells
Protein data vs. concentration (both β and δ); the same for amino acids and nucleic acids
Origin of α-dispersion in membranes (counter ion induction, related to excitation, internal structure or chemical relaxation?)

The precise origin of the δ-dispersion and the relative contribution of bound water and polar side chain rotation requires further clarification.

The theory of counter ion relaxation has so far been developed only under fairly restricting assumptions and further work is required to fully assess the contribution of counter ions to the low-frequency data.

There are still more data to be gathered for amino acids, proteins and nucleic acids, particularly as functions of concentration and field strength. Macromolecular interactions may affect dielectric data at typical biologic concentrations. There is need to better understanding of various relaxations typical of nucleic acids. There is a particular need to gather data as functions of field strength in order to find out where macromolecular dielectric saturation occurs. This is needed to assess the possibility that high field strength levels as may be applied with pulsed fields may go beyond saturation levels and perhaps cause denaturation, a possibility which is judged by the writer to be remote but not entirely impossible.

Last, but not least, the origin of the α-dispersion needs further elaboration. We should learn to assess the relative contributions of counter ion effects, dielectric effects in excitable membranes caused by time-dependent sodium and potassium and due to possible chemical relaxation effects in membranes, and dielectric effects due to intracellular membrane structures.

It is quite possible that such work may provide further insight into the various ways in which electric fields of whatever frequency and magnitude may reversibly and irreversibly affect biological structures.

In the meantime the past work and the internal consistence achieved can be summarized in some fairly simple conclusions. The electric data are entirely consistent with biologic matter consisting of membranes surrounding and being surrounded by intracellular and extracellular fluids which contain macromolecules. There is no doubt that the large part of the water contained is "free" since both dielectric data and conductivities at microwave frequencies are essentially those of electrolytes containing biopolymers and the characteristic frequencies in the γ-range are identical for tissues and free water. From this well supported picture emerge the following conclusions of interest here:

1. At frequencies above those characteristic of the α-dispersion all biological membranes have a fairly frequency-independent capacity of about 1 μF/cm^2, with the precise value varying between 0.5 and 1.5 μF/cm^2. This capacitance range which is presently unchallenged corresponds, say at 3 GHz, to an impedance of about 50 microohms. For a current density of about 3 mA/cm^2, i.e., a current density which corresponds to a flux of 10 mW/cm^2 in tissues of a typical 3 GHz resistivity of 100 to 200 ohm-cm, an alternating membrane potential of only 0.15 μV is induced. This value is easily 1000-fold, if not 10 000-fold, smaller than potentials which are reported to cause effects on excitable membranes.

2. All the properties reported above are "linear" ones in the range of potentials at which they were studied, i.e., the reported dielectric constants and conductivities are independent of field strength at field strength levels of interest at this meeting. Membrane data change at first at field strength levels which almost compare with those corresponding to a typical resting potential of 70 mV, i.e., at imposed field levels of the order of 100 kV/cm. Biological macromolecules, judging from the restricted body of data available, are linear up to field levels of many kV/cm. This means that the energies which are imparted by thermal collisions are far greater than those which can be applied with fields of the order of several V/cm. The present knowledge therefore does not indicate any possibility of denaturation by the field strength levels of interest here. Moreover, the characteristic frequencies quoted are smaller than those of microwaves, making it thereby unlikely for biopolymers and membranes to respond to microwave frequencies.

3. The electric data known so far are without exception a reflection of relaxation effects, and there is no indication of any resonance behavior. For example the data on biopolymers are consistent with those of polar molecules surrounded by a medium which has the viscosity of water, i.e., a viscosity high enough to preclude any resonance type of behavior. The same is true for the membrane data so far reported. The abundant data therefore do not lend support to the concept that microwaves may induce resonance effects which may somehow denature and cause irreversible damage.

FORCES CAUSED BY EM-FIELDS

While the above-discussed electric properties provide much insight into the mode of interaction of alternating electric fields, they cannot reveal readily whatever mechanic effects may be imparted. It has been known for quite some time that not only DC fields but also alternating ones can evoke forces which may or may not be significant. The study of the manifestations of these forces has been of considerable interest over a number of years in our laboratory. The well-known pearl chain formation effect and the orientation of nonspheric particles are some of the effects which have been studied (Fig. 3).

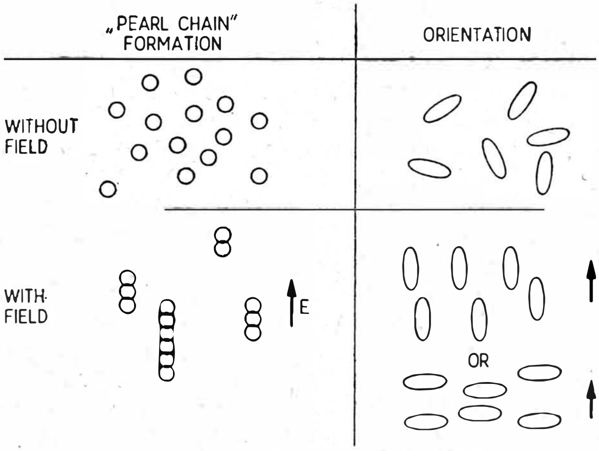
„PEARL CHAIN" FORMATION
ORIENTATION
WITHOUT FIELD
WITH FIELD
E
OR

Fig. 3. Schematic presentation of some effects of alternating electric fields on particle and cellular arrangements.

In general it may be said that such forces become significant in comparison with random thermal ones if the ratio of the electric potential energy of the system considered or its change as the observed effect takes place is larger than the thermal energy. This ratio is proportional to the expression given in Figure 4 and the proportionality

$$\frac{L(P)}{L(T)} \sim \left| \frac{\varepsilon_p^* - \varepsilon_a^*}{\varepsilon_p^* + 2\varepsilon_a^*} \right|^2 \frac{R^3 E^2}{KT} \varepsilon_p$$

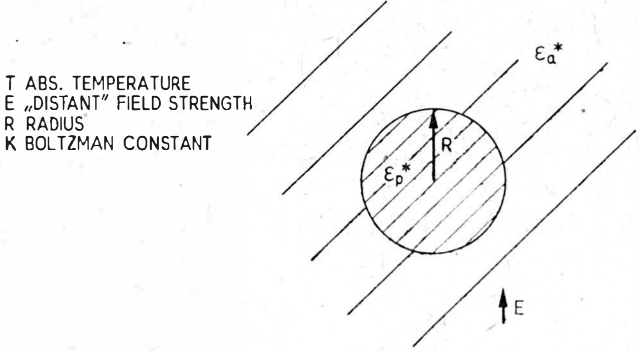
T ABS. TEMPERATURE
E „DISTANT" FIELD STRENGTH
R RADIUS
K BOLTZMAN CONSTANT
εa*
εp*
R
E

Fig. 4. Ratio of electric potential energy L(P) to thermal energy L(T) of a particle of a complex dielectric constant E_p^* and radius R in a medium of complex dielectric constant E_a^* and exposed to a field E.

constant depends on the particular phenomena considered. For example in the case of the movement of a particle in an inhomogeneous field, termed "dielectrophoresis" by Pohl, the proportionality factor characterizes the inhomogeneity of the field and the force generated is given by

$$F = 2\pi R^3 \varepsilon_p \frac{\varepsilon_p^* - \varepsilon_a^*}{\varepsilon_p^* + 2\varepsilon_a^*} \cdot \operatorname{grad} (E_a^2)$$

It is apparent from the expressions given that the threshold field strength to evoke such effects as mentioned changes inversely with the square root of the volume of the particle exposed. Indeed, typical cellular dimensions of the order of some μm require field values of several hundred volt/cm, i.e., values which have been reported in the literature for erythrocyte pearl chain formation, *E. coli* orientation, etc. On the other hand large unicellular organisms have recently been subject to investigation in our laboratory and respond dramatically if the field strength is only of the order of 1 V/cm. It is therefore indicated that forces which are caused by alternating fields are not likely to be significant at the molecular and microscopic cellular level unless huge field strength values are assumed, values which are so large that the accompanying thermal effects would be overwhelming. However, on a macroscopic level these effects may well be significant. We have pointed out before on several occasions that the phenomenon of hearing pulsed microwave fields may well be explained by the forces rhythmically applied to the middle ear structures as the field is turned on and off. Since only the strength of the applied field dictates the force generated, the observation by several investigators that the peak power is the important parameter is readily unterstood. This observations is in no contradiction to our statement that for "steady state" effects, such as pearl chain formation or orientation, the effect of a pulsed field can at most equal that of a continuous field of the same average power (see Fig. 5).

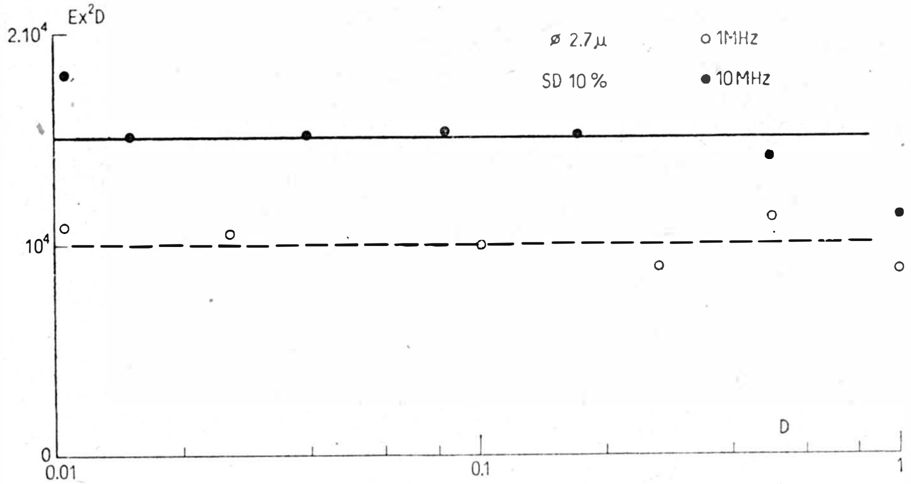

Fig. 5. Threshold of pearl chain formation as function of duty cycle D. The ordinate is given in terms of the product of D with the square of the peak field strength. The data provide experimental evidence that the phenomenon of pearl chain formation cannot respond to a pulsed field more readily than to a continuous field of the same average power (S. Takashima and H. P. Schwan, submitted for publication).

In summary: The electric properties of biologic systems are well known and understood. This understanding does not indicate so far the existence of nonthermal effects at the molecular or cellular level. However, forces which can be generated by the application of alternating fields (field-evoked forces, dielectrophoresis, electromechanical effects as various authors have termed them) deserve consideration and may well be responsible for the phenomenon of "hearing" pulsed fields and, hence, some of the behavioral effects reported in the 1 to 10 mW/cm² range.

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INTERACTION BETWEEN MICROWAVE AND MILLIMETER-WAVE ELECTROMAGNETIC FIELDS AND BIOLOGIC SYSTEMS: MOLECULAR MECHANISMS

K. H. Illinger

Department of Chemistry, Tufts University, Medford, Massachusetts, U.S.A.

INTRODUCTION

The objective of this discussion is to treat the interaction between electromagnetic radiation and the molecular components of biologic systems, in order to delimit the possible coupling mechanisms with EM fields which may lead to an alteration of the energetics and/or dynamics of the molecular system. The latter is deemed a prerequisite for any consequent biologic effects; possible interactions at the systems level, with a salient coupling mechanism to forms of biologic organization beyond the molecular level, are not considered here.

Salient aspects of the interaction between RF and microwave radiation and biological systems have been summarized inter alia by Schwan (43) and Michaelson (34). The subsequent discussion treats some aspects which complement and extend their conclusions regarding primary coupling mechanisms between EM fields and biologic systems. The motivation for the treatment of certain heuristic model systems is to delimit the probability and to define the nature of any biologic effects expected to arise as a result of these physical coupling mechanisms. The current intractability of the theoretical problem, whose physics has been sketched in the above, forces almost complete reliance, in the assessment of possible biologic effects, on empirical evidence obtained from experiment. Analysis of experimental findings in terms of a heuristic model may serve to correlate and generalize the observed behavior.

Although the structural variety of molecular systems of biological importance is myriad, the degree of conformational variety and organization implicit in certain model structures representative of a general biopolymer may elucidate the general problem. One such system is that of the poly-α-amino acids; a model system on which considerable structural, spectroscopic, and dielectric information is available is poly-(α-benzyl L-glutamate) or PBLG. This molecule is a representative poly-amino acid, with polar side-chains attached to the polymer backbone, and capable of undergoing a helix-coil transition. It is of interest to discuss the degrees of freedom of this complicated system, and to represent its interaction with EM fields.

Characteristic of biopolymeric systems whose helical form consists of a concatenation of polar helical turns, with a dipole moment of 1—5 D per unit turn, are very large values of the total dipole moment in the helical conformation, of the order of 10^3 D (23, 24, 26), while the statistical average of the dipole moment in the random coil form is essentially zero. Hence, it is expected that the helical form of molecules such as PBLG will exhibit overall rotational relaxation and couple to an RF field; such a relaxation process has in fact been found (53) in the region near 10 kHz, for PBLG of weight-average molecular weight of 150 000. Furthermore, while the detailed theory (44, 45, 46) of dielectric relaxation induced by chemical reaction is of some complexity, one may expect that the very large changes in dipole moment for the helix-coil transition will lead to a second absorption mechanism. In fact, PBLG absorbs MW radiation near 1 MHz as originally predicted (44) and subsequently found experimentally (32, 47); this absorption is associated with a correlation time of 5×10^{-7} s for the helix-coil transition (5, 30, 35, 47, 54). It is of interest to mention that, while the electrical susceptibility undergoes large changes in the helix-coil transition, analogous changes in the magnetic susceptibility of this diamagnetic system exhibit an upper limit of less than one percent (9). It is expected that the polar side chains attached to the PBLG backbone will exhibit rotational relaxation in the range 1—10 GHz, since the magnitude of their group-rotational relaxation times lies near 10^{-10} — 10^{-9} s. Although the value of the relaxation time will differ in the two cases, both the helix and the coil conformations should share this relaxation mechanism. For the random-coil form, one may surmise that a rather wide distribution of relaxation times will occur, owing to the variety of the intermolecular environments that the side-chains will experience, tending to broaden the frequency spectrum of this absorption. A summary of the RF and microwave absorption frequencies of PBLG, including those of two mechanisms to be discussed in the following section, is as follows:

mechanism	**frequency**	**correlation time**
rotational diffusion[a]		
overall rotation of helix	10 kHz	10^{-4} s
group-rotation of side chains	1—10 GHz	10^{-10} — 10^{-9}
chemical relaxation	1 MHz	5×10^{-7}
quasilattice vibration[a]	10—1000 GHz	—
libration motions	100—1000 GHz	—
X—H...Y vibration	3000 GHz	—

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[a] function of the degree of helicity and molecular weight.

QUASI-LATTICE VIBRATIONS OF BIOPOLYMERS

The two rotational diffusion mechanisms cited above are expected to show the inverse temperature dependence of the relaxation time τ characteristic of relaxation phenomena. There exists another mechanism for MW absorption in an ordered, extended structure such as the α-helix which lies at the borderline of relaxation processes and is perhaps best described as a quasilattice vibration of the helix perturbed by molecular collisions. The complete analysis of the 3N-6 normal modes of vibration, where N is the total number of atoms, of a biopolymer is a formidable task since N is of the order of 10^4 for molecular weights of the order of 10^5. Considerable effort has been expended in the attack on the general theoretical problem of the normal-coordinate analysis of polymers in the unperturbed state (1, 10, 11, 12, 20). The spectrum of normal modes may be divided into three regions, associated with widely different force constants; namely, (a) group vibrations, involving vibrational motion of small numbers of atoms, with force constants of the order of 1—10 mdyn/Å (1 mdyn/Å = 10^5 dyn/cm), and associated frequencies of the order of 10^3 cm^{-1} (1 cm^{-1} = GHz) infrared; (b) vibrations which correspond to the distortion of the unit which comprises the building blocks of the overall polymer, e.g. a single turn of the helix in a helical system, with force constants in the case of hydrogen-bonded helices such as PBLG $\sim$ 0.1 mdyn/Å 34.37 and frequencies $\sim$ 100 cm^{-1} or 3000 GHz; (c) vibrations which comprise distortion of essentially the entire polymer and which, for a quasi-infinite system, would be the lattice vibrations. It is the latter which are of interest in the microwave- and millimeter-wave region.

While the coupling of EM fields E_0 to the rotational degree of freedom of a molecule depends on a nonvanishing value of $\mu E_0 \cos\vartheta$, where μ is the permanent molecular (or segmental) dipole moment and Θ is the angle of orientation of μ in the field, the vibrational degree of freedom will be active in absorption of EM fields if the change of the total dipole moment with vibrational distortion, represented by the normal coordinate Q_k, is nonvanishing, $(\vartheta\mu/\vartheta Q_k) \neq 0$. In the case of the quasilattice vibrations of biopolymers in the α-helical form, longitudinal vibrations are expected to produce substantial values of the dipole-moment derivative. If the vibration can be treated as a harmonic oscillator, the associated intensity of absorption of EM fields has the form, $K_k \sim \omega_k (\vartheta\mu/\vartheta Q_k)^2$, where ω_k is the harmonic frequency, and A_k is independent of the temperature (18). The frequency of the vibration, ω_k, for the isolated molecule is a constant and can be estimated by a simplified normal-coordinate analysis which treats the distortion of one helical segment against the other as the distortion of a two-mass point system, or, in a more refined model, as the distortions of a helical-staircase model, where the helical backbone is connected by rungs parallel to the axis of the helix comprised of the X—H...Y hydrogen bonds. Perturbation of a molecular vibration, even of rather small force constant, by molecular collisions is expected to be considerably smaller than that of an overall or segmental rotation. As a first approximation, one may stipulate the quasi-lattice vibrational frequency ω_k to be independent of the average thermal energy of collisions, i.e. independent of T, but affected by the mean value of the intermolecular potential.

A microwave absorption in the range between 1 and 20 GHz for PBLG of MW $\sim 10^6$, independent of T, has been observed (8), and interpreted in terms of a simple classical model. The α-helix may be approximated classically as a continuous spring with an effective force constant associated with the X—H...Y distortions. The principal longitudinal vibrational frequency can then be estimated by: $\omega_p = (s/L)\,(k/m)^{1/2}$, where s is the pitch of the helix, with $2\,\pi s$ being the distance between successive turns of the helix, k the effective force constant per unit term determined from the X—H...Y force constant (40), L the length of the helix, and m the effective mass. Although this classical model is a drastic simplification of the quasilattice vibration problem and is applicable only to the simple α-helix, it correlates with the magnitude of the observed MW absorption of PBLG. A more complete analysis of the quasilattice vibrations of ordered biopolymer structures provides the dependence of the frequency ω_k on the molecular weight. Since ω_k will decrease in a monotone fashion with increasing MW, a range extending from the millimeter-wave into the centimeter-wave region is to be expected for this absorption process, depending on the MW of the system. The damping of the vibrational excitation by molecular collisions will be considerably less effective than rotational diffusion in a fluid; accordingly, the predictions of dielectric relaxation theory are not appropriate to this interaction. Although the α-helix is a special case of very high symmetry (helical screw-axis throughout the molecule) and biopolymers, such as proteins (55), have in many cases rather irregular three-dimensional structures, where regularity of three-dimensional structure and nonvanishing dipole-moment derivatives for quasi-lattice vibrational distortion occur, the coupling mechanism discussed here may become operative. Irregularity in structure may be thought of as leading to destructive interference of vibrational modes and a consequent broad, featureless spectrum of lattice modes, in contrast to the discrete spectrum of a highly regular structure. Finally, it is of interest to point out that the distortion of the hydrogen bridges in the α-helix, parallel to the helix axis, which generates the active longitudinal vibrations near 10 GHz, has no direct counterpart in double-helical structures such as that of DNA since in this case the hydrogen-bonded subunits lie essentially perpendicular to the helix axis. This is not to say that DNA exhibits no longitudinal quasilattice vibrations, but that the hydrogen-bonded subunits are not involved in these vibrations in the same fashion as those of the α-helix (56). In particular, vibrational distortion of the hydrogen-bridged system in DNA is primarily associated with perpendicular quasilattice vibrations, expected to lie above 100 cm^{-1} and essentially independent of the degree of polymerization, whereas distortion in the α-helix system contributes both the far-infrared frequency near 100 cm^{-1} and the microwave frequency range near 1 cm^{-1}, the latter being a function of molecular weight.

DIELECTRIC SATURATION IN BIOPOLYMER SYSTEMS

For simple monomeric molecular systems with permanent dipole moments $\sim$ 1 D = $= 10^{-18}$ esu cm and polarizability anisotropies one has for the ratio of the field-interaction energy to the average thermal energy the inequalities for attainable laboratory field strengths E_0 and ordinary temperature T. The average thermal energy dominates

$$|\alpha_{\parallel}-\alpha_{\perp}| \sim 10^{-24}\,cm^3 \qquad [1]$$

over the field interaction, and the ordinary (non-saturation) approximations of dielectric theory hold. For biopolymeric systems with dipole moments $> 10^3$ D and/or polarizability anisotropies $> 10^{-20}$ cm^{-3}, the status of the above-mentioned inequalities is altered to approach unity for attainable field strengths E_0.

$$(kT)^{-1}\langle \mu \mathcal{E} \cos\Theta \rangle_{Av} \ll 1, \quad (kT)^{-1}\langle |\alpha_{\parallel}-\alpha_{\perp}|\, \mathcal{E}_0^2 \rangle_{Av} \ll 1 \qquad [2]$$

The theory of dielectric saturation has been discussed by a number of authors (23, 24, 37, 38, 39). Saturation of the electrical birefringence (Kerr effect) at fields of several kV/cm has been studied for PBLG (25, 40) and tobacco mosaic virus (19), and virtually total dielectric saturation of PBLG has been achieved in static (21) and 1 msec pulsed fields (13) with fields up to 60 kV/cm. The shift of the relaxation time for overall rotation of PBLG and of ethyl cellulose has been reported in fields up to 10 kV/cm (4).

The acquisition of large values of the dipole moment and the polarizability anisotropy in ordered structures of polymers made up of polar monomeric units is a general phenomenon. As a first approximation, the total dipole moment for a polymer consisting of N monomeric units with the z-component of the monomeric moment, μ_z, (parallel to the symmetry axis of the polymer) is simply:

$$\mu_{\parallel} = \sum_i (\mu_z)_i \cong N\mu_z \qquad [3]$$

The polarizability anisotropy at zero frequency may be written as:

$$\alpha_{\parallel}-\alpha_{\perp} = \left(\alpha_{\parallel}^{el}-\alpha_{\perp}^{el}\right) + \left(\alpha_{\parallel}^{vib}-\alpha_{\perp}^{vib}\right) \cong \alpha_{\parallel}^{el} + \sum_{k_{\parallel}} \omega_{k_{\parallel}}^{-2} \left(\partial \underline{\mu}/\partial Q_{k_{\parallel}}\right)^2 \qquad [4]$$

where α_{II}^{el} and α_{I}^{el} are components of the electronic polarizability, α_{II}^{vib} and α_{I}^{vib} the vibrational components, which may be written in terms of the vibrational dipole-moment derivates and frequencies (56). The superposition of monomer moments longitudinally produces the large value of μ_{II}. The fact that the field along the z axis sees a concatenation of the N electronic chromophores leads to $\alpha_{II}^{el} >> \alpha_{I}^{el}$, and the preponderance of low-frequency vibrational modes in the parallel direction leads to

$\alpha_{\parallel}^{vib} >> \alpha_{\perp}^{vib}$; hence, the polarizability anisotropy at zero (or microwave) frequencies considerably exceeds that just below electronic frequencies.

Certain structures other than highly symmetrical biopolymers may be expected to show pronounced dielectric saturation effects, for reasons similar to those which altered the status of the ratio of thermal-energy to field-interaction energy in the ordered biopolymer cases discussed above. One such situation is the decoupling of Zwitterion molecules from a micelle, whose average dipole moments is essentially zero, to form the non-micellar state with associated large values of μ. Pulsed-field measurements of fields up to 100 kV/cm and duration $\sim$ msec have been carried out (22) on egg lecithin, a phospholipid of the type found in cell membranes. It is found that near 10 kV/cm application of a series of pulses is sufficient to disrupt the micelles to essentially mono--molecular aggregates. In translating measured dielectric saturation effects into expected behavior *in vivo,* attention must be given to the effect of the environment of the system (e.g. solvent in the laboratory measurement) on the intermolecular forces and the dielectric properties.

SUMMARY AND CONCLUSIONS

A basic physical description of the dynamics of a molecular system in the presence of perturbations by an EM field and by intermolecular forces was provided.

Information indicating that the natural EM background in the biosphere at microwave- and RF-frequencies in orders of magnitude below the power levels assiociated with technological and/or scientific applications was provided. In contrast, the natural background at VLF, ELF and zero-frequency (static) fields in the biosphere is of the same order of magnitude as certain technical applications.

A detailed model, at the level of organization representative of the molecular components of biological systems, of mechanisms of interaction between microwave and millimeter-wave EM fields and biological systems was delineated. From these considerations, it would appear that irreversible effects arising from the perturbation of rotational diffusion in biological fluids by external EM fields in the RF and centimeter-wave region, at normal *in vivo* temperatures, have a low probability at field strength below saturation levels. The existence of quasilattice vibrations in extended biopolymetric structures (e.g. the alpha-helix) indicates the possibility of damped resonant interactions between millimeter-wave and far-infrared EM fields and biological systems.

Irreversible saturation effects in biological fluids are expected only at (static) field strengths of the order of $kVcm^{-1}$, in helix-coil transitions of certain biopolymers and in micelle-random-Zwitterion transitions.

The problem of microwave EM field-induced proton shifts in the hydrogen bonds of biopolymers was discussed; such field-induced proton shifts, and hence possible associated genetic-code alterations, are improbable for systems such as DNA.

APPENDIX

DESCRIPTION OF THE MOLECULAR SYSTEM

The time-evolution of the energy of a molecule in the presence of collisional perturbation by other molecules and of perturbation by an electromagnetic field may be characterized by the (Hamiltonian) energy operator H (t):

$$H(t) = H_0 + V(t) + H_f(t) \qquad [5]$$

Here, H_0 represents the (time-independent) energy operator for the isolated molecule, separable to first approximation, into the electronic, vibrational, and rotational degrees of freedom:

$$H_0 \cong H_0(el) + H_0(vib) + H_0(rot) \qquad [6]$$

V(t) is the (time-variant) potential energy due to molecular interaction, and $H_f(t)$ is the interaction operator due to the EM field. If the form of V(t) and $H_f(t)$ is accurately known, H(t) is defined and the energy of the system can be predicted, in principle, by solution of the time-dependent Schroedinger equation:

$$\frac{i}{\hbar} \frac{\delta}{\delta t} \Psi(r,t) = H(r,t)\,\Psi(r,t) \qquad [7]$$

where Ψ (r, t) is the wave function and $\hbar$ = h/2, where h is the Planck constant. In Equation [7], the dependence of the energy operator and of the wave function on both the time, t, and all the spatial coordinates of the n-particle system, r = (r_1, r_2,...r_n), has been articulated. In practice, direct solutions of Equation [7], even for simple forms of the intermolecular potential V(t), as well as for arbitrarily large field interactions $H_f(t)$ are not available. Progress toward solving Equation [7] can be made in the limiting case where both V(t) and $H_f(t)$ are small compared to H_0, since it can then be assumed that V(t) + $H_f(t)$ can be treated as a perturbation operator and employed, to varying degrees of approximation, within the framework of perturbation theory and with the solutions of the time-independent Schroedinger equation,

$$H_0(r)\ \Psi_0^n(r) = E_0^n\ \Psi_0^n(r) \qquad [8]$$

to obtain the energies of the perturbed system. Here, the eigenvalues E_0^n are the unperturbed energies of the system. For complex molecules, Equation [8] can be solved to fair accuracy, albeit with computational effort which increases rapidly with the total number of electrons in the molecule. In spite of the computational intractability of the theoretical framework traced in the above, it may serve as the basis of a semi-quantitative discussion.

It is of interest to examine first the nature of the molecular interactions represented by the intermolecular potential energy V(t) in Equation [5]. Whereas the total energy of an unperturbed molecule in its ground state is of the order of 100 kcal mole^{-1} per chemical bond, intermolecular forces generate interaction energies V of the order of 0—5 kcal mole^{-1} during collisions at average intermolecular separations near STP. Schematically, the instantaneous intermolecular potential V(r, t′) can be constructed by the superposition of several terms, (15) e.g.,

$$V(r,t') = V_{rep}(r) + V_{dis}(r) + V_{es}(r) + V_{ind}(r) + V_{hb}(r) \qquad [9]$$

at an instant of time t′. Terms on the rhs of Equation [9] which pertain to any atomic or molecular system are the repulsive term $V_{rep}(r)$ and the so-called dispersion term $V_{dis}(r)$. The former arises from the symmetry constraints imposed upon the electric charge distribution in an n-electron system by the Pauli exclusion principle; in effect, the energy of any atomic or molecular system will increase if the interelectronic distances, r_i—r_j, are decreased below the equillibrium distance. Thus, any two atoms or molecules colliding with sufficient kinetic energy will be repelled by a force whose integral is the term V_{rep}; this interaction potential is short-ranged, i.e. operative only at small interaction distances, and can be approximated by functions of the form $+Ae^{-kR}$

or, less accurately, $+A'/R^{12}$, where R is the average intermolecular distance, and A, A′, and k are parameters. The foregoing statement becomes invalid in the case of a chemically-reactive collision, in which case collision may form a new molecule, thereby changing H_0 and altering the energetics of the system by a magnitude commensurate with forming a chemical bond. Chemically-reactive collisions will be excluded in the present discussion. The competition between $V_{rep}(R)$ and attractive terms in Equation [9], which leads to a characteristic value of the interatomic or intermolecular distance S for which $V = 0$, defines a molecular radius. While compression of mean distances between electrons invariably leads to $V(R) > 0$ for short-range interactions, R being of the order of a few angstroms, correlation of electronic motion in colliding atoms or molecules leads concomitantly to V(R) becoming attractive at slightly longer ranges. The latter is represented by $V_{dis}(R)$, a potential term which, owing to its relation to the polarizability, is said to arise from the dispersion force; the leading term in a reasonably accurate expression of $V_{dis}(R)$ has the form $-B/R^6$, for a simple two-atom interaction. For interactions between atoms, $[V_{rep}(R) + V_{dis}(R)]$ represents the total instantaneous potential V(R, t); its variation with time is defined by the values of the distance, R(t), which are consistant with a given collision path.

For molecules, additional terms in Equation [9] become nonvanishing. Whereas all atoms are spherically symmetrical, and thus have vanishing electrical multipole moments, molecules will exhibit some non-zero multipole moments. The set of possible multipole moments (charge, dipole moment, quadrupole moment, octupole moment, etc.) appear as molecular constants in the expression for the electrostatic potential, $V_{es}(R)$, in Equation [9]. In fact, $V_{es}(R)$ can be expressed as an inverse power series in the intermolecular distance R, with constants in this series containing combinations of multipole-multipole, and multipole-induced-multipole interactions between the two molecules. An important aspect of the electrostatic, as well as the induction, terms in V is that $V_{es}(R)$ and $V_{ind}(R)$ are functions of the angular orientation of one molecule with respect to another, allowing positive and negative values of V depending upon the orientation. The term $V_{ind}(R)$ in Equation [9] describes the induction of multipoles in a molecule via the perturbation of permanent multipoles of an adjacent molecule. Finally, in systems containing H atoms chemically bonded to atoms such as O, N, F, and permitting the proximity (within 1—2 Å) of non-bonded atoms (O, N, F), an additional, strong interaction results in the formation of the hydrogen bridge X—H...Y, which may be said to contribute to V a term $V_{hb}(R)$. This term is separated from the other terms in V because the nature of the hydrogen-bond interaction is not adequately expressed in the form of any of the other intermolecular forces, although it is frequently implied that the hydrogen bridge is essentially an electrostatic interaction. The hydrogen bridge (often, less descriptively, called the hydrogen bond) is an extremely important intermolecular interaction in biological systems, as well as in such liquids as H_2O. Because the energy of the hydrogen bridge is extremely sensitive to the X—H...Y angle, this interaction exhibits even stronger angular characteristics than the electrostatic and induction interactions.

In a typical molecular system relevant to a biological entity, all of the molecular interactions summarized in Equation [9] and briefly traced above will be operative. In fact, the secondary and tertiary structures of biologically important molecules, in particular biopolymers, are strongly determined by intermolecular forces. The three-dimensional architecture of biologically important molecules is at once flexible and programmable in that a multitude of configurations of the isolated molecule are attainable by internal rotation about C—C, C—N and C—O bonds. The potential energy for such intramolecular conformational alterations is of the same order of magnitude as the intermolecular interaction energies given by Equation [9]. As a consequence, there exists a fairly large set of conformations of slightly different energies for a biopolymer, each component of which has a slightly different stability depending on its intermolecular environment. Equilibria among different conformers have been studied extensively, and the effect of thermodynamic variables, such as pressure and temperature, on such equilibria are reasonably well understood. The dynamics of conformational equilibria are less well characterized, and the time evolution of conformations in the open, steady-state systems that characterize real biological entities is not fully understood to date.

The dynamics of molecular systems of biological interest are affected by the thermodynamic variables of state which characterize their macroscopic environment and by any external potentials, such as EM fields. Given the viability of known biological systems in the presence of natural background of temperature, pressure, gravitational fields and non-ionizing radiation, it is of interest to inquire into the EM background in the biosphere, before considering the effect of man-made perturbations.

NATURAL BACKGROUND OF NON-IONIZING RADIATION IN THE BIOSPHERE

Apart from certain natural sources of ELF and VLF fields, to be touched upon later, the natural background of EM non-ionizing radiation in the terrestrial biosphere arises from (a) radiation from the sun and (b) reradiation from the earth. Although transmission through the atmosphere modifies the solar spectral irradiance R (1) at the surface of the earth, the envelope of radiation flux (i.e. the upper limit of R (1) as a function of the wavelength 1) is quite accurately described as a blackbody distribution, with T = 5700°K (2). Similarly, the terrestrial reradiation can be treated as arising from a blackbody at 288°K. Characteristic of the blackbody model is that the total radiant energy emitted over all wavelengths is cT^4, where c is the Stefan-Bolzmann constant, and that the wavelength associated with the maximum value of R (1) occurs at $1_{max} =$ $= 2898$ m/T. The latter relation predicts maximum values for R (1) at 0.5084 µm and 10.06 µm for the solar and the terrestrial blackbody radiation, respectively. Measured solar spectral irradiance at 38 000 ft shows a maximum R (1_{max}) = 208.5 mW cm^{-2} µm^{-1} at 0.480 microns wavelength, consistent with a solar constant (total radiation emitted at all wavelengths) of 135.1 mW cm^{-2} or 1.938 cal cm^{-1} min^{-1}. Measurements at 1, 10, and 20 microns wavelength give values of 74.6 mW^{-2} 2.5 × 10^{-2} mW cm^{-2}, and 1.6 × 10^{-3} mW cm^{-2}, per unit micron wavelength interval, respectively. The percentages of the solar constant associated with shorter wavelength radiation at 1, 10, and 20 microns are 69.42, 99.935, and 99.9893 percent, respectively. It is evident from these considerations that the natural blackbody radiation background in the terrestrial biosphere at wavelengths beyond the far-infrared (beyond 100 microns) is below microwatts cm^{-2} in the long-wavelength limit. R(1) falls off essentially exponentially with wavelength, so that the natural background at microwave and RF frequencies is several orders of magnitude below the far-infrared flux.

Ionization processes in the atmosphere, produced mainly by cosmic radiation and natural terrestrial radioactivity, produce electric fields of the order of 100—200 V m^{-1}; under disturbed weather conditions, fields of 10^3 V m^{-1} are observable. Emissions from lightning further provide ELF fields in the region 3—300 Hz and VLF fields in the region 1—10 kHz; then, former may produce resonances in the earth-ionosphere cavity with typical resonance frequencies near 10 Hz for the first few modes. In the RF and microwave regions, the only natural background is the superposed blackbody distributions of solar and terrestrial radiation. For a bandwidth of 1 MHz, thermal or "Johnson" noise produces a power output of the order of 10^{-14} W in amplificatory systems at 300°K. Power sources for scientific purposes thus have power outputs many orders of magnitude above the background. As a result, the EM field perturbation term in Equation [5] may be taken, to extremely good accuracy, to arise purely from the externally applied field, neglecting the natural background, in the microwave and RF regions.

MOLECULAR DYNAMICS IN THE PRESENCE OF EM FIELD PERTURBATION

In principle, the prescription of the time-dependent energy operator in Equation [5] permits complete formulation of the problem of the dynamics of a molecular system being perturbed simultaneously by intermolecular forces and an external EM field. It will be assumed that an adequate expression for $H_f(t)$ can be written in the form:

$$H_f(t) \cong E_0^{int} \cdot \underline{\mu} \left[e^{ivt} + e^{-i\omega t} \right] G(t,\omega) \qquad [10]$$

Here, ω is the angular frequency of the EM field, and $G(t, \omega)$ is a function which describes the time-profile of the EM field. For CW radiation, $G = 1$; for AM or FM modulated fields, $G(t, \omega)$ takes on the appropriate form. More general fields, containing more than one frequency, can be written as a superposition of terms as in Equation [10]. E_0^{int} is the amplitude of the internal field, i.e. the effective field at the molecule, and μ is the dipole-moment operator. The problem of computing accurate values for the internal field in a general dielectric is a formidable one; however, for the present purpose it will suffice to consider it of the same order of magnitude as the macroscopic field in the dielectric. This argument does not include the attenuation of the external macroscopic field as it penetrates through a dielectric. The magnetic vector of the EM field has been neglected in Equation [10], since magnetic interactions, except for ferromagnetic and paramagnetic systems, are much weaker than electric--field interactions (25). It should be noted, however, that the magnetic vector of an EM field is capable of inducing eddy currents in a conducting dielectric which, in turn, produce macroscopic electric fields in the dielectric. This effect, of particular importance at frequencies below the microwave region, requires knowledge of the detailed radiation pattern of an EM source for both the electric and magnetic vector.

An accurate description of the dynamics of a molecular system under the perturbations summarized in Equation [5] requires, aside from the form of $H_f(t)$ in Equation [10], an accurate formulation of the time-dependent intermolecular potential energy $V(r, t)$. Although the description of a molecule in the gas phase undergoing collisions and interacting with an EM field can be treated, to varying degrees of approximation, by scattering theory, (19, 51) the solution of the problem for condensed states provides serious difficulties. In particular, some real biological entities are inhomogeneous systems with characteristics intermediate between those of a simple liquid and those of solides. Thus, it is expected that the ordinary quasi-continuum models for the dielectric properties of fluids are not completely adequate for the general problem of the perturbation of biodynamic systems by EM radiation. Nevertheless, some qualitative features of the simple theories are expected to provide a guide toward actual behavior of these systems. At ordinary temperatures in simple fluids, molecular interaction reduces the lifetimes of individual rotational eigenstates to such an extent that, owing to the indeterminacy relation $\Delta E \Delta t > \hbar$ (where Δt is the lifetime of an eigenstate and ΔE is the associated indeterminacy in the energy), the rotational degree of freedom becomes quasi-classical. (The translational degree of freedom is quasi-classical even in a dilute gas, since the spacings of the translational energy levels are within ΔE as determined by the lifetime of translational states, even at very low pressures.) As a result, the interaction of the rotational and translational degree of freedom in a simple fluid with an EM field is characterized by a relaxation process. In some solids, the rotational degree of freedom, as well as presumably certain inversion modes, can remain quantized (36). Furthermore, in certain cases, at sufficiently low temperatures, quantized rotational motion may persist in the liquid state (3). For a simple fluid, the molecular constant which characterizes the dynamics of the interaction to first order is the rotational diffusion constant or the correlation time for rotational diffusion. Extensive theoretical and experimental work (7, 14, 17, 48) on simple fluids and simple solids has been carried out to determine rotational relaxation behavior. The orders of magnitude of rotational correlation times of many molecular and of representative intramolecular segments capable of internal rotation have been measured. Although the prediction *ab initio* of rotational correlation times is a task that still confronts dielectric theory, empirical and semi-empirical schemes are available to correlate experimental findings on simple fluids (49), polymer solutions and colloids.

In spite of the extensive treatment of dielectrics, a complete predictive theory for the perturbation of biodynamical systems by microwave and millimeter wave EM radiation cannot be said to exist. Conformational changes in biologically active molecules can, in principle, be induced by EM radiation. A crucial question is the relaxation toward the biologic steady-state of such induced changes, if any, within the time scale of biologically significant processes. In particular, the extent to which biologically active molecular systems (and their reactions and/or transport at biomolecular surfaces, membranes, etc.) are describable by a quasi-solid rather than quasi-homogeneous liquid, remains an incompletely solved research problem. The accuracy of the description of the medium or substrate in which a biologically active molecule is found *in vivo* may be crucial to an adequate model for the interaction with EM fields. The latter requires an accurate description of the intramolecular potential for conformational change as well as the intermolecular potential V(r, t) *in situ*. Finally, although the effect of (all but extremely large) external fields on the equilibrium constants of chemical and conformational equilibria is expected to be small, the actual *in vivo* biodynamical system is a (non-equilibrium) open, steady-state system with finite relaxation times. All these aspects render an accurate description of collisional and EM perturbations of real biological systems difficult but challenging.

Although the foregoing discussion has hardly paved the way toward computational elucidation of Equations [5-9], the formalism presented may aid in the conceptual appreciation of the treatment of actual systems. In fact, the crucial question as to whether collisional perturbations in a given system are associated with adiabatic or diabatic processes may be examined numerically with the aid of a criterion for adiabaticity (33):

$$A = \left| \int_0^{\delta} (\Delta E_{ab})^{-1} \left(\frac{dH}{dt}\right)_{ab} \left[\exp\left(\frac{i}{\hbar} \int_c^{\delta} \Delta E_{ab}\, dt''\right) dt' \right] \right| \ll 1 \qquad [11]$$

Here, ΔE_{ab} is the energy difference between the levels of energy E_a and E_b being bridged by the EM photon, and $(dH/dt)_{ab}$ is the time derivative of the total Hamiltonian, Equation [5], appropriate to the states *a* and *b*, and δ is of the order of the duration of a collision. It is enlightening to perform an order-of-magnitude evaluation of the integral A. In the case of a molecule in the dilute gas, the average value of the intermolecular potential, V(t), in Equation [5]), is small, tending toward zero as the pressure decreases. If the relative velocity of the perturber and the absorber is 10^4 cm s^{-1}, the duration of a typical collision in the gas phase is 10^{-12} s; the intermolecular potential varies roughly between 10^{-13} erg and zero. If we consider $(dH/dt)_{ab}$ to be constant during the collision (i.e. a triangular interaction potential), the value of A to first order is given by: $A = (1/h)(V_0/\omega_{ab}) = 10^{14}/\omega_{ab}$. It is apparent that transitions for which the adiabetic assumption holds cannot be less than 10^{14} cp s^{-1} in frequency. This frequency is in the infrared region; in the microwave region, the adiabetic approximation is clearly inapplicable. Experimental confirmation of this fact exists in studies of the effect of microwave power saturation on line widths in the spectra of gases. This result leads to the assumption of the very opposite of the adiabatic approximation: one can assert that gas-phase collisions are sudden, and strongly diabatic, in the time scale of rotational transitions (50). Molecules in a liquid experience an average intermolecular potential several orders of magnitude larger than that operative in the dilute gas; superimposed upon this average are excursions in H(t) due to individual collisions. In the solid, the rotational and translational degrees of freedom of individual molecules are in general transformed into lattice vibrations, although molecular rotation or group rotation may persist in certain cases. Whilst analysis via Equation [11] in the case of condensed states is rendered difficult because of the lack of detailed knowledge of (dH/dt), recent direct experimental measurements (27) of the lifetimes of vibrational states in simple fluids confirm the magnitude of 10^{-11} s, indicating that the regime of strongly adiabatic interactions lies considerably above 1 cm^{-1} (30 GHz). This order of magnitude for the lifetime of molecular states is consistent, via the uncertainty principle, with an indeterminacy of the energy of the order of 1 cm^{-1}, corroborating the fact that molecular transitions in the microwave region in condensed states are nonresonant, whereas those in the infrared are strongly resonant, and those in the far-infrared represent an intermediate case.

RF AND MICROWAVE ABSORPTION IN BIOPOLYMERS

The microwave absorption of biological systems is dominated by the intense rotational relaxation of H_2O, centered at 17.2 GHz, corresponding to a relaxation time of 9.24×10^{-12} s at 20°C, with an E_{max} near 35. The H_2O absorption, which fortuitously fits with great accuracy the form of the complex dielectric constant function predicted on the basis of a single relaxation time, provides efficient attenuation of a microwave EM field in the GHz region into a biological entity.

FIELD-STIMULATED PROTON SHIFT IN THE H-BRIDGES OF BIOPOLYMERS

Since the tertiary structure of many molecular systems of biological importance is closely connected with the existence of hydrogen bridges between pairs of atoms within the molecule, the effect of possible motion of the proton in such environments on the fidelity of molecular replication, in particular that of DNA and hence the genetic code, has been frequently discussed. Since the small mass of the proton imparts a finite tunneling rate ($<<$ lifetime of an individual) to its motion, the question of spontaneous proton tunneling in DNA has been given some attention (28, 29) and appeared to have been corroborated by an early quantum-mechanical study of the energy surface of the DNA base-pairs as a function of the position of the three protons linking the bases (42). The limited basis set of electronic wave functions employed in that study *inter alia* conspired to imply a double-minimum potential for the motion of a single proton across one of the three hydrogen bridges in the guanadine-cytosine base-pairs of DNA. A subsequent study (6), with state-of-the-art sophistication in electronic computing, permitted considerable refinement of the basis set of electronic wave functions and numeral techniques in general. The cuts through the potential surface pertaining to the motion of a single proton across one of the hydrogen bridges in the DNA base pair were found, on the basis of this computation, to show a single minimum. Simultaneous motion of two protons, involving two hydrogen bridges, is associated with a double-minimum intramolecular potential energy function in the case of formic acid, HCOOH, (circular) dimer (6); even the refined computations in Ref. (6) were not deemed sufficiently accurate by their authors to include or exclude the possibility of such a double minimum for simultaneous motion of two protons in the DNA base-pair problem. Viewed conservatively, their conclusions render doubtful any field-induced single-proton transfers in DNA by RF and microwave EM radiation, although field-stimulated proton shifts have been invoked (38) in analyzing dielectric saturation in aliphatic alcohols (31).

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EFFECTS OF MICROWAVE IRRADIATION IN VITRO ON CELL MEMBRANE PERMEABILITY

S. Barański, S. Szmigielski and J. Moneta

Military Institute of Aviation Medicine, Warsaw, Poland

Biologic effects of irradiation of living organisms with very high frequency electromagnetic waves were demonstrated several years ago (for review, see ref. 3). Nevertheless, the mechanism of extrathermal biologic effects of microwaves in living organisms remains still unknown, although various hypotheses have been proposed. Paramagnetic resonance (9), ionic conductivity (10) and changed dielectric characteristics of certain compounds (7, 14) are suggested as the phenomena leading to the extrathermal effects of microwave irradiation. Only a few papers have been published on the effect of microwave irradiation on isolated cells *in vitro,* although a rather strong cytopathic effect of microwaves have been demonstrated (11, 16).

In view of the above it seemed interesting to evaluate the effect of microwave irradiation on cell and lysosomal membranes. The cell membrane, because of its morphologic structure (5, 12, 18) and function (13) should be highly susceptible to the action of any factor leading to changes in dielectric parameters of protein molecules. As increased permeability, the displacement of potassium ions from cells to the extracellular fluid and the disturbed function of the sodium-potassium pump, followed by higher permeability for larger molecules, the well-known signs of cell membrane injury (15) it seemed interesting to test these phenomena in cells undergoing microwave irradiation *in vitro.*

MATERIAL AND METHODS

Erythrocytes. Erythrocytes were isolated from heparinized (50 I.U./ml) rabbit venous blood by centrifugation and washing in saline three times. The cells were suspended in chemically clean saline, containing no potassium, to form a 10% suspension and were irradiated in thin-wall Plexiglas tubes with continuous electromagnetic waves of 10 cm length at 1, 5 and 10 mW/cm^2 power densities, in each case at the far field. The cell suspensions were irradiated during 15, 30, 60, 120 and 180 minutes, the temperature of the suspensions being checked during the whole period of irradiation. The control erythrocytes were stored at room temperature. In irradiated and control RBC suspensions the following estimations were performed:

1. Concentration of hemoglobin in the supernatant (after centrifugation at 3000 rpm during 15 min) with use of the Beckman colorimeter;
2. Osmotic resistance curve at NaCl concentrations of 0.9%, 0.8%, 0.7%, 0.6%, 0.5%, 0.4%, 0.3%, 0.2% and 0.1%. The amount of hemoglobin liberated was measured with Beckman's colorimeter and compared to erythrocytes suspended in a 0.1% solution of NaCl.
3. Potassium concentration in the supernatant by the titration method of Pincussen (8).

Granulocytes. Rabbit granulocytes were isolated from the peritoneal cavity 8 h after an infusion of 0.5% glycogen in saline (6) and suspended in heparinized saline 50 I.U./ml). The suspensions were diluted with saline to obtain 10^6 cells/ml and the percentage of granulocytes was checked on slides stained according to the May-Grunwald-Giemsa method. Suspensions containing at least 90% of mature granulocytes were used for further studies. Granulocytes were irradiated in thin-wall Plexiglas tubes with continuous 10-cm waves at 1 or 5 mW/cm² during 15, 30 and 60 minutes, in each case at the far field. In control and irradiated suspensions of granulocytes the following estimations were performed:

1. Supravital staining with 0.1% nigrosin (6) and observation of the percentage of stained (dead) cells in a light microscope. 500 cells were counted in each case.

2. Activity of acid and alkaline phosphatases and lysozyme (muramidase) in supernatants after centrifugation at 5000 rpm during 15 min at 4°C (in plastic tubes). The phosphatases were determined according to the King-Armstrong method (for details see ref. 6), lysozyme by means of the turbidimetric technique of Litwack (4) based on lysis of lyophilized *Micrococcus lysodeikticus.* The activities of the above enzymes were compared to the activity found in supernatants of granulocytes (10^6/ml) frozen and thawed three times and centrifuged, as above. Activity in frozen/thawed suspensions was estimated as 100% and the results obtained in irradiated suspensions were expressed as a percentage of the above value.

RESULTS

Hemoglobin concentration, osmotic resistance and concentration of potassium are presented in Figures 1 and 2.

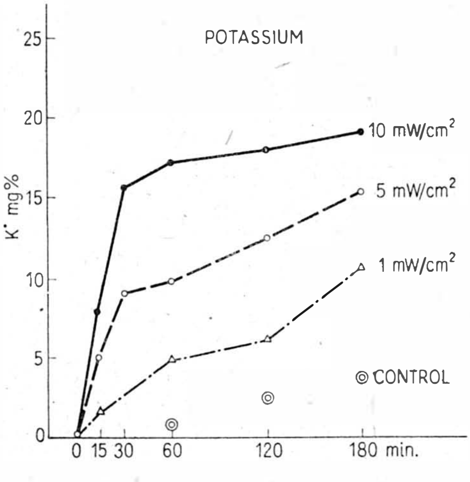

Fig. 1. Concentration of hemoglobin in the supernatant of suspensions of erythrocytes irradiated with microwaves.

Increased permeability of erythrocyte cell membranes to hemoglobin was observed only after irradiation at 1 mW/cm² during 60 min.

Osmotic resistance of erythrocytes irradiated with microwaves decreased during irradiation (Fig. 1), being time- and dose-dependent. During the first two hours of

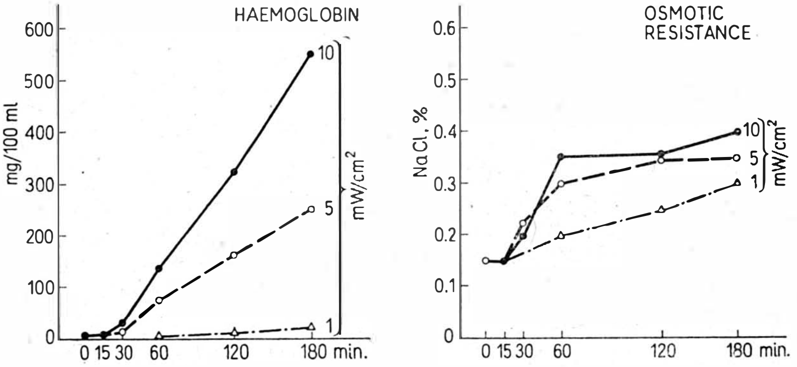

Fig. 2. Osmotic resistance of erythrocytes and concentration of potassium in supernatants of erythrocytes irradiated with microwaves.

irradiation at 1 mW/cm2 no significant changes, as compared to control solutions, were observed. After 120 min of irradiation, total hemolysis occurred already at 0.3% NaCl, while at higher power densities osmotic resistance markedly decreased after 30 minutes (Fig. 1).

Changes in potassium metabolism were the earliest observed disturbances in erythrocytes irradiated with microwaves. After only 15 min of irradiation at 1 mW/cm2 power density a significant increase in potassium concentration in the supernatant was noted (Fig. 2). The values were still higher after longer lasting irradiation or after irradiation at 5 or 10 mW/cm2 power density.

A marked increase in the percentage of dead (stained with nigrosin) granulocytes was observed only in suspensions irradiated at 5 mW/cm2 (Fig. 3). After a 60-min irradiation at this power density, about 80% of granulocytes showed diffuse staining

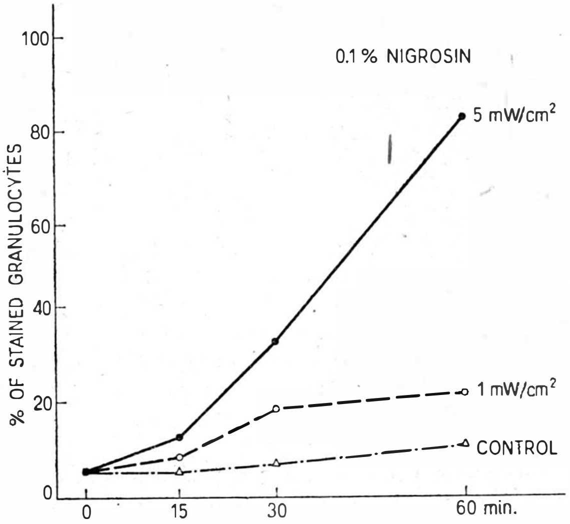

Fig. 3. Staining of granulocytes irradiated with microwaves with 0.1% nigrosin (percentage of stained cells per 500 cells).

with nigrosin, while in suspensions irradiated at 1 mW/cm² only about 20% of granulocytes were stained, the last figure being close to the value observed in control solutions, not irradiated with microwaves.

Activities of acid and alkaline phosphatases and lysozyme in supernatants of granulocytes irradiated with microwaves are summarized in Figure 4.

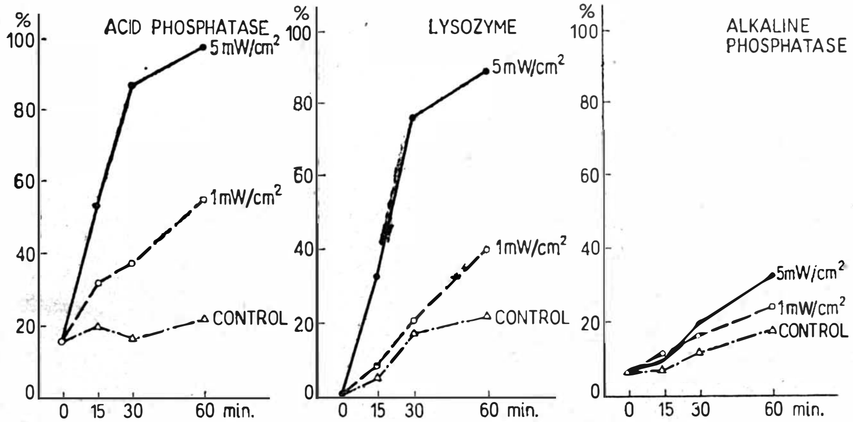

Fig. 4. Activity of acid and alkaline phosphatases and lysozyme in the supernatant of suspensions of granulocytes irradiated with microwaves.

After a 60-min irradiation with 10 cm waves at 5 mW/cm², about 85% of the whole activity of acid phosphatase and lysozyme were liberated from granulocytes and found in the supernatant, while only about 45% of the whole activiy of alkaline phosphatase were liberated from cells under this condition (Fig. 4). Liberation of higher amounts of acid phosphatase and lysozyme, as compared to alkaline phosphatase was also noted in suspensions irradiated at 1 mW/cm² (Fig. 4). In control suspensions not irradiated with microwaves only trace activities of all the three enzymes were found.

DISCUSSION

Irradiation of erythrocytes and granulocytes *in vitro* resulted in marked injury of cell membranes. After 15 minutes irradiation with 10 cm microwaves at 1 mW/cm², the power density that causes no thermal effect, increased potassium concentration in the supernatant was observed. This was followed by decreased osmotic resistance of the cells and increased cell membrane permeability for hemoglobin at higher power densities. Injury of the cell membrane function seems to be time- and dose-dependent. In granulocytes irradiated at 5 mW/cm² a rapid increase of the percentage of dead cells and liberation of lysosomal enzymes (acid phosphatase and lysozyme) from the cells was seen, while at 1 mW/cm² partial liberation of the hydrolases was the only phenomenon observed during 60 minutes of irradiation.

Lack in the literature of reports concerning the effect of microwave irradiation on the cell membrane function suggested that it would be best to begin by testing the most simple experimental system — isolated erythrocytes and granulocytes *in vitro*. The cell membrane of these cells does not differ in its function and morphology from that of other cells (2, 17). In granulocytes two distinct forms of intracellular granules, differing in their morphology and function were found (1, 4): azurophilic granules containing lysosomal hydrolases, among them acid phosphatase and lysozyme, and specific granules containing alkaline phosphatase. Damage of the above granules results in liberation of their enzymatic "markers" into the cytoplasm or extracellular fluid, depending on the character and intensity of cell injury (1, 4). The amount of enzymes liberated from granulocytes proved to be a useful test for measuring the cytopathic effect and its specifity (4). The results obtained in granulocytes irradiated *in vitro* with microwaves suggest a damaging effect of higher power densities (5 mW/cm^2) for lysosomes, while under these conditions the liberation of enzymes localized in specific granules (alkaline phosphatase) is much smaller.

On the other hand, the disturbed function of erythrocyte cell membranes was observed already after 15 minutes of irradiation at 1 mW/cm^2. The increased permeability for potassium ions, observed under these conditions, seems to be the effect of the disturbed function of the sodium-potassium pump. This system is very active in erythrocytes (2) and a high activity of the sodium-potassium activated adenosine-triphosphatas (Na-K-ATP-ase) was demonstrated in red blood cells (2). A longer time of irradiation of erythrocytes in microwave fields resulted in decreased osmotic resistance and increased permeability of cell membranes to hemoglobin. These phenomena are probably the consequence of earlier disturbances in the sodium-potassium pump and the signs of an irreversible injury of the cell membrane, leading to the death of cells. Under similar conditions and time of irradiation (30—60 min at 5 mW/cm^2) about 80% of granulocytes showed staining with 0.1% nigrosin. Staining with nigrosin, widely used for determining cell vitality (6), depends on cell membrane permeability for large molecules and the positive results suggest an irreversible injury of the cell membrane.

In view of the results obtained it is our feeling that irradiation of cells *in vitro* with microwaves at non-thermal power densities causes injury of the cell membrane function and the efflux of potassium from cells seems to be the first sign of disturbances in the cell membrane function.

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ASSESSING MICROWAVES AS A HAZARD TO THE EYE — PROGRESS AND PROBLEMS*

R. L. Carpenter, E. S. Ferri and G. J. Hagan

Northeastern Radiological Health Laboratory, Bureau of Radiological Health, Food and Drug Administration, Department of Health, Education and Welfare, Winchester, Massachusetts, U.S.A.

In 1948, Daily et al. (9) and Richardson et al. (19) independently reported development of opacities in the lens following exposure of the eyes of rabbits or dogs to microwave radiation. Subsequent research has both confirmed their findings and extended our knowledge of the action of microwaves on the lens. Much remains to be learned regarding the relation of factors such as radiation frequency, power density, frequency of successive exposures and intraocular temperature to the degree of lens damage. More studies are needed on biochemical, metabolic, cellular and fine-structure changes associated with microwave-induced opacities. We particularly need well grounded information on how microwaves affect the human eye.

Many investigators have reported development of lens opacities after one exposure of the eye at various frequencies from 0.8 to 10 GHz (2, 3, 4, 5, 6, 7, 8, 15, 20, 21, 22, 25). When the eye was at any distance from the transmitting source, opacities characteristically developed in the posterior subcapsular cortex of the lens. However, when microwaves were transmitted directly by having the eye closely applied to an aperture in a diaphragm which terminated a waveguide (8) or to the corneal-fitted end of a dielectric waveguide transition terminating either a waveguide or a coaxial conductor (5) then the opacities which developed were in the anterior subcapsular cortex, as has been reported also for experimental electric cataracts (10, 11).

In most experiments involving microwave irradiation of the eye, the radiation source was a dipole antenna backed by a reflector and the eye was positioned only a few inches from it. The radiation was largely confined to the animal's head and the field was a near-zone one, with consequent difficulties in attempting to assess the level of microwave power acting on the eye. Additionally, in much of the earlier work, instrumentation suitable for reliable measurement was not available. As a result, investigators had to resort to describing the conditions under which irradiations were performed or, using instruments, providing values which, unfortunately, were not applicable to the conditions of the near-zone field. In view of these circumstances, it is futile to compare the results of experiments performed in many different laboratories, although the attempt has been made (18).

Even without reliable power measurements, it was still possible to determine, for any given output of a particular microwave source, the minimal single exposure period required to induce opacity formation in the lens. With power outputs expressed in some term of relative measurement common to all the experiments of a given series,

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* Presented by Dr. R. L. Elder.

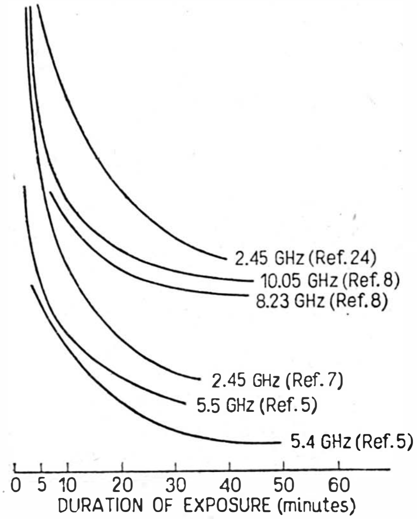

Fig. 1. Shapes of curves showing time-power thresholds for induction of lens opacities in the rabbit eye at various microwave frequencies. (Note: Ref. 24 should read Ref. 25).

these minimal single exposure periods could yield a curve showing time and power thresholds for the induction of lens opacities by single irradiations of the eye. Although data derived in different laboratories could not be expected to be identical with respect to time-power relations, the threshold curves reported by three different laboratories and covering several frequencies — 2.45, 5.4, 5.5, 8.2, and 10 GHz — were similar in shape. (Fig. 1).

The threshold curve for a given experimental series was also useful for identifying specific time and power combinations which constituted subthreshold exposures, incapable of producing changes in lens transparency. Consequently, it became possible to test the effect on the lens when a subthreshold exposure was repeated at regular intervals. If multiple exposures, separate in time and each incapable of causing opacity formation, were to result finally in a lens opacity, there would be demonstrated a cumulative, or additive, effect. A number of such experiments were performed and did, indeed, demonstrate that episodes of irradiation which apparently do not permanently harm the lens when experienced only once may cause lasting damage when they are repeated daily or even weekly (7, 8).

In our most recent experiments of this nature, eyes of non-anesthetized mature New Zealand white rabbits were irradiated two inches from a dipole antenna at 2.45 GHz, continuous wave, one hour daily for 20 consecutive days. Defining this arbitrarily as chronic irradiation, we sought to find the lowest power level which would most consistently cause development of lens opacities. The results of 59 such experiments are summarized in Table 1.

The power levels there referred to were measured by a Narda Model 8100 electromagnetic radiation survey meter (1) with its sensing probe placed in the exact position to be occupied by the cornea of the rabbit's right eye during its irradiation. Although the figures in the left-hand column represent the meter readings in mW/cm^2, they may not be accurate for the near-zone field conditions of the experiments, inasmuch as the probe does not respond to a radial component of the electric field. Nevertheless,

Table 1

Lens opacities resulting from consecutive daily exposures of the right eye to 2.45 GHz radiation

Power density mW/cm²	No. Animals	No. Exposures 1 hour each	Positive response	
			No. Animals	Percent
50	10	20	0	0
80	9	20—24	1	11
90	10	20	1	10
100	10	18—32	4	40
110	10	21—30	4	40
120	10	13—20	8	80

the various power measurements are relative and afford a basis for comparison among these experiments.

Lens opacities developed in only 4 out of 10 experiments performed at the 100 and 110 mW/cm² levels but with an increase in power to 120 mW/cm², opacities developed in 8 of 10 experiments. A one-hour exposure at this power level was truly subthreshold, for when tested in seven experiments, no lens opacities resulted (Table 2). Ten anesthetized rabbits were subjected at the same power to single exposures ranging from $1^3/_4$ to $5^1/_2$ hours and with only two exceptions, no opacities were observed in the irradiated eyes nearly a year later.

When the eye is irradiated, it is a matter of days before the first sign of opacity formation is seen as discrete small granules scattered along or near the posterior lens suture. These small opacities are the end result of a complex series of events initiated within the lens when it has absorbed microwave power. It is important to learn what happens in the lens during this latent period; fortunately, a start has been made.

Table 2

Lens response resulting from single continuous exposures of right eye to 2.45 GHz radiation

Power density mW/cm²	No. of cases	Exposure duration (hours)	Right eye		Left eye	Post-irradiation observation days
			Opacity	No change	No change	
120	7	1	0	7	7	30—324
120	1	1.75	0	1	1	20
120	2	2	0	2	2	11
120	1	2.5	0	1	1	10
120	2	3	0	2	2	343, 363
120	1	3.5	0	1	1	340
120	1	4	1*	0	1	348
120	1	4.5	1**	0	1	329
120	1	5.5	0	13—20	1	315

* Small central opacity after 137 days; no change thereafter.

** Small central opacity after 173 days; no change thereafter.

Merola and Kinoshita (17) and Kinoshita et al. (14) made biochemical studies of rabbit lenses removed at different intervals following cataractogenic exposure of the right eye. The first identifiable change in the irradiated lens, occurring after 6 hours and before 18 hours post-irradiation, was a decrease of approximately 23 percent in lens ascorbic acid. This change took place some days before the first signs of an opacity would have been seen. There was no change in the ascorbic acid level of the aqueous humor and when isolated non-irradiated lenses were heated to the same temperature and for the same period of time as the lenses of the irradiated eyes experienced, the ascorbic acid concentration remained unchanged.

Van Ummersen and Cogan (24) employed autoradiography to investigate the effect of microwaves on the lens epithelium and found that in lenses which had been exposed to cataractogenic doses, there occurred in the epithelium an inhibition of DNA synthesis and a decrease of mitotic activity. This inhibition was most marked in the period of one to five days following irradiation, after which recovery gradually took place but not until two weeks after irradiation had DNA synthesis and mitotic activity returned to normal.

It has already been mentioned that most of the reported experiments on microwave induction of lens opacities were performed with the eye in the near-zone field, where the radiation pattern is complex and measurement of power density is not a reliable procedure. This objection does not apply to the far-zone field, where a properly designed and calibrated instrument can measure power density in the field exactly where the animal's eye will be subjected to irradiation. However, other problems arise. One is that while the eye as the target organ is being irradiated, the animal is at the same time being subjected to whole body irradiation and its possibly lethal effect.

Another problem is that an object in a microwave field, unless it completely transmits or absorbs the energy incident upon it, will tend to perturb that field. This field perturbation, in turn, may profoundly alter the power density incident on the eye. To ascertain the extent to which a microwave field might be altered through perturbation by the body of a rabbit, we undertook some experiments, using a Narda Model 8100 Electromagnetic Radiation Survey Meter (1), which has a cylindrical sensing probe 23 mm in diameter. Radiation was 2.45 GHz frequency, continuous wave, from a 17.3 db. standard gain horn into an anechoic chamber 2 m high, 2 m wide and 4.15 m long.

With only the probe in the chamber, 150 cm away from the horn, power was adjusted for a reading of 60 mW/cm^2 on the survey meter. The probe was then placed in exactly the same position but after it had been passed through the head of a freshly sacrificed rabbit from which both eyes and all tissues between had been removed. The rabbit was then positioned in the chamber as if for irradiation, with the sensing part of the probe where the cornea of the right eye would have been. With no change in transmitted power, the meter reading was now only 35 mW/cm^2. The presence of the animal thus so perturbed the field that the power density at the position of the eye was reduced by approximately 40 percent. This measurement was made with the rabbit's ears in their normal erect position. When the ears were fastened down against its back, power density changed to only 21 mW/cm^2.

To conduct a more detailed study of the effect of field perturbation, we designed and constructed apparatus for scanning and continuously recording power density along any horizontal line across the width of our anechoic chamber. By recording a series of such scans separated 2.5 cm in the vertical plane and transferring the data to graph paper, we could construct a plot showing equal power contours for all or any part of the vertical plane. We first scanned a vertical plane one meter square and 150 cm distant from the radiating horn. The transmitted power was adjusted to

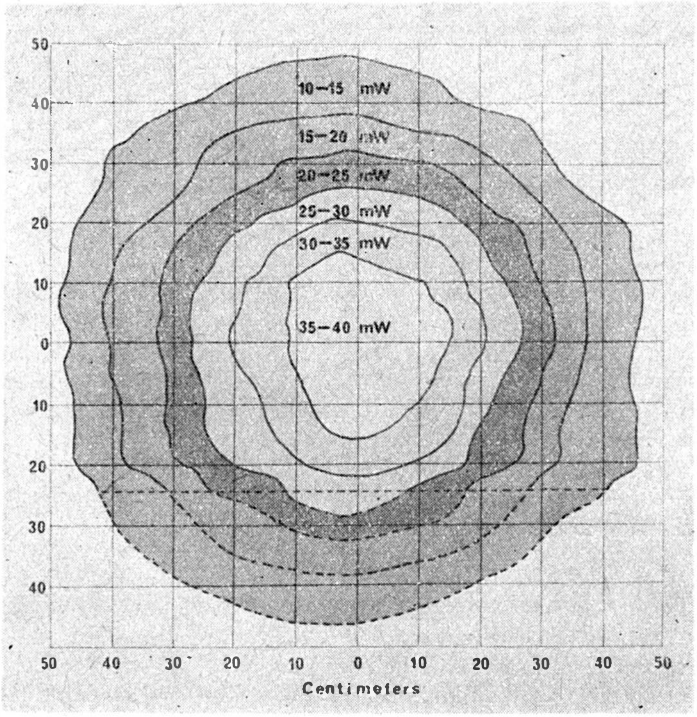

Fig. 2. Contours of equal power density for a vertical plane one meter square in a free field.

40 mW/cm² at the center of the plane, a point coincident with the projected geometrical axis of the horn. When power contours differing by 5 mW/cm² were plotted from these scans, the resultant plot (Fig. 2) represented the power distribution of a plane wave under the approximately free field conditions of our anechoic chamber. It resembled an archery target, with concentric circular zones decreasing in power density in a regular manner from 40 mW/cm² at the center to 10 mW/cm² at the periphery.

When the process was repeated at the same radiated power but with a rabbit placed just behind the vertical scanning plane, its right eye in line with the center of the field, the resulting plot was quite different (Fig. 3). In place of the symmetrical arrangement around a 40 mW/cm² central region was a haphazard pattern of irregular zones of differing power densities. In front of the eye, the power density was 50 mW/cm², a 25 percent increase. When the same animal was scanned in the same place and in the same position but with its long ears taped down instead of erect, the resulting plot was still irregular but the pattern was different (Fig. 4). Power density in front of the eye was now 60 mW/cm², representing an increase of 50 percent over the free field value. With the ears down, the pattern of field perturbation seemed conducive to reducing the hazard to the eye, as compared to the situation when the ears were erect. This agreed with the findings obtained when the survey meter probe was passed through the head to measure the power density at the plane of the cornea.

We also determined that cages, animal restrainers, or supports made of plastic, other than expanded polystyrene, can perturb the field and thereby alter the conditions of the experiment. We are forced to conclude that power density should be reported only as a measurement taken in the radiation field where the experiment is to be conducted

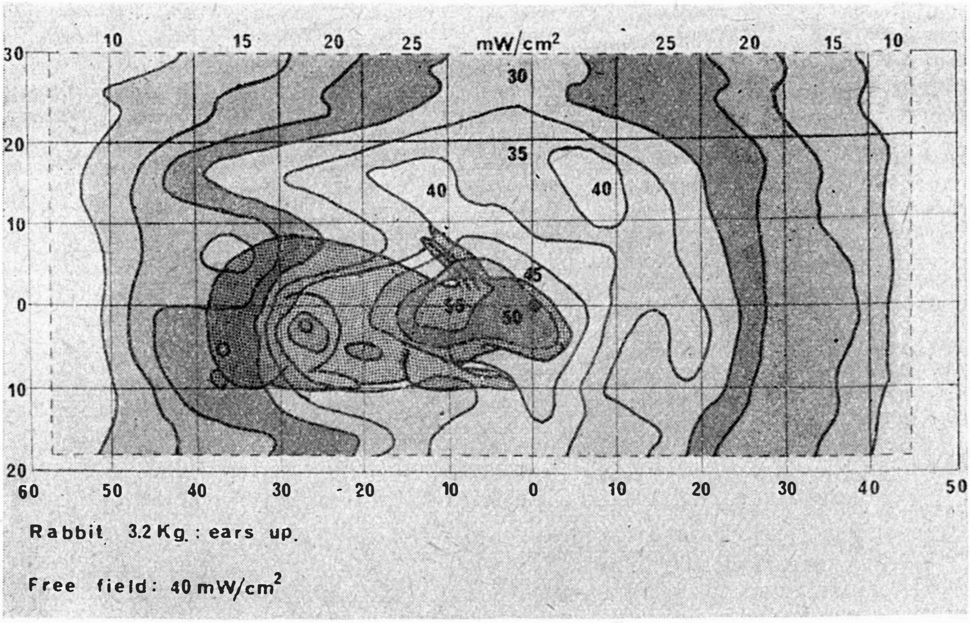

Fig. 3. Contours of equal power density made under the same conditions as was Figure 2 except for the presence of a rabbit just behind the measured plane. The animal's ears were in an erect position.

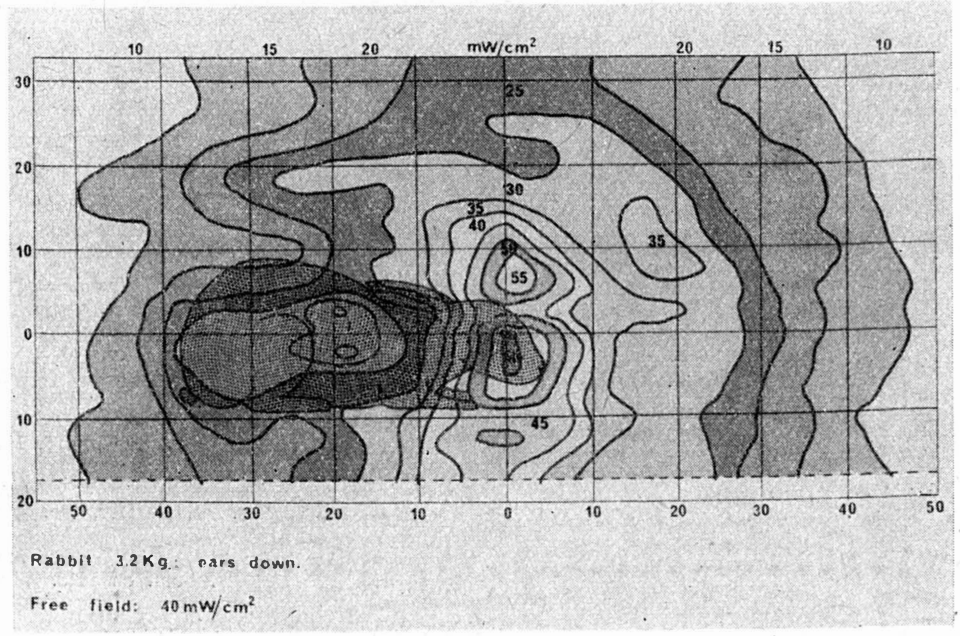

Fig. 4. Contours of equal power density made as in Figure 3 but with the rabbit's ears held flat against the body.

and made in the absence of all perturbing factors, including the experimental animal. The size, shape and orientation of the animal are unpredictable factors.

Unfortunately, we cannot validly extrapolate to man the results of animal experiments. Even though a time-power threshold can be established for the induction of opacities in the rabbit eye, we cannot assume that the same conditions will produce a similar effect in another species. We have no reason to think that the human eye possesses a special immunity to the effects of microwaves but we have no information as to whether this radiation offers a greater or a lesser hazard to it than to the rabbit eye. We do not know how the human eye interacts with the microwave field or how its response to irradiation may be affected by field perturbations caused by the human head or the human form.

Our most insistent problems are in the field of dosimetry. Despite the many improvements in the reliability of electromagnetic survey meters for the evaluation of fields external to the body, we still must hope for an instrument sufficiently miniaturized so that it can be implanted in living tissues and there measure fields and absorbed power without modifying the field.

As of now, we do not know of a case in which microwave radiation has been the proven cause of a human cataract. The fact that a man develops posterior subcapsular cataracts and that at some previous time in his life he had been, or may have been, exposed to microwaves does not automatically establish a cause and effect relationship. Cases of presumed microwave cataract have been reported in the literature (2, 12, 13, 16, 23, 26, 27) but in no instance has convincing evidence been offered that microwaves were actually the causative agent. This is not to deny the possibility that they could have played that role but simply to point out that the supporting evidence which has been offered does not necessarily lead to that conclusion. In the assessment of microwave radiation as a hazard to the human eye, we must expect that any attempt to establish, *ex post facto,* a clear cause and effect relationship in suspected or alleged human cases will encounter difficulty. Nevertheless, we must insist that the scientific scrutiny accorded these cases be no less demanding than that applied to conclusions based on animal experimentation.

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EXPERIMENTAL MICROWAVE OCULAR EFFECTS

B. Appleton

Ophthalmology Service, Walter Reed Army Medical Center, Washington D.C., U.S.A.

Albino rabbits were exposed to microwave radiation of the eyes under varying experimental conditions: acute single and chronic multiple exposures: two different frequencies (1700 MHz and 3000 MHz); anesthetized and unanesthetized animals; exposure of the head or eyes only and exposures involving more of the body; and

Tabela 1

One-year follow-up of single microwave exposures

Rabbits	Power density	Duration of exposure	Acute effects	Chronic effects
3	100 mW/cm²	15 minutes	0	0
3	100 mW/cm²	30 minutes	0	0
3	200 mW/cm²	15 minutes	0	0
3	200 mW/cm²	30 minutes	0	0
3	300 mW/cm²	15 minutes	+	0
3	300 mW/cm²	30 minutes	lethal	
3	400 mW/cm²	15 minutes	+	0
3	500 mW/cm²	15 minutes	(3)	0
3	Controls		0	0

Frequency: 3000 MHz CW
Anesthesia: none
New Zealand albino rabbits (5lb)
Exposure to left eye placed one foot beyond focus .

Table 2

One-year follow-up of five consecutive daily exposures

Rabbits	Power density	Duration of exposure	Acute effects	Chronic effects
3	100 mW/cm²	30 minutes	0	0
3	100 mW/cm²	60 minutes	0	0
2	200 mW/cm²	20 minutes	0	0

Frequency: 3000 MHz CW
Anesthesia: none
Left eye at one foot past focus of dish antenna
Albino rabbits (5lb)

pulsed as well as continuous waves. In addition, power density of levels varying from 25 mW/cm² to 500 mW/cm² were used.

A summary of the results of these experiments is contained in Tables 1 through 4.

Table 3

Two-month follow-up of multiple microwave exposures

Rabbits	15 min daily exposure	Power density	Acute effects	Chronic effects
5	30	50 mW/cm²	0	0
5	30	100 mW/cm²	0	0
5	30	200 mW/cm²	0	0
5	30	300 mW/cm²	+	PSCI
5	30	400 mW/cm²	+	CAT.
5	14	500 mW/cm²	+	CAT.

3000 MHz CW
Anesthesia: ketamine HCl
Left eye at focus of elliptical dish antenna
New Zealand albino rabbits

Table 4

Two-month follow-up of multiple microwave exposures

Rabbits	15 min daily exposure	Power density	Acute effects	Chronic effects
5	30	50 mW/cm²	0	0
5	30	100 mW/cm²	0	0
5	30	200 mW/cm²	0	0
5	30	300 mW/cm²	+	PSCI
5	30	400 mW/cm²	+	CAT.

Frequency: 3000 MHz pulsed
Anesthesia: ketamine HCl
Left eye at focus of elliptical dish antenna
New Zealand albino rabbits

In addition, an experiment in which several rabbits were exposed simultaneously to 25 mW/cm² to the whole front of the body resulted in no deaths and no ocular damage, but the same experiment performed at 50 mW/cm² resulted in death of all the rabbits so exposed.

DISCUSSION

In would be virtually impossible within the resources of any of our present microwave research facilities to explore experimentally all the combinations and permutations of these variables: 1) number of exposures, 2) duration of exposures, 3) wavelength, 4) power level, 5) duty cycle, 6) head only versus whole body exposures, and species of experimental animal. Nevertheless, from the data at hand, some tentative conclusions can be drawn.

CONCLUSIONS

It appears that in the rabbit the lethal power level is somewhere between 25 mW/cm^2 and 50 mW/cm^2 if the front or one side of the animal is irradiated. But if the body is protected by shielding, or if the radiation is directed at the head only, the threshold for ocular damage appears to be around 300 mW/cm^2; and the results of these experiments appear to offer little support for the hypothesis that repeated subthreshold exposures cause significant cumulation of damage. It also appears from these experiments that exposure to power levels approximately one order of magnitude below cataractogenic levels is sensed as an extremely noxious stimulus, probably thermal, causing the animal to struggle violently, to remove itself from the field.

The few initial observations gleaned from similar experiments using dogs (just recently initiated) appear to be roughly in quantitative agreement with those from the rabbit experiments, indicating an encouraging similarity with respect to microwave ocular effect between the two experimental models of the human case, despite their species-related differences from one another.

THE EFFECTS OF MICROWAVES ON HUMAN LYMPHOCYTE CULTURES

W. Stodolnik-Barańska

Institute of Biostructure, Medical Academy in Warsaw, Warsaw, Poland

Numerous reports indicate that microwave exposure may induce changes in the peripheral blood picture and the hematopoietic system both in man (2, 5, 9, 11) and in experimental animals (2, 3, 4, 9, 11). It should be stressed that long-term, low-dose exposure may induce peripheral lymphocytosis, stimulation of lymphopoiesis and anomalies of nuclear structure and mitotic abnormalities in lyphocytes and erythroblasts in guinea-pigs and rabbits (2, 3, 4, 6). In view of these data it seemed interesting to investigate the effects of exposure to microwave radiation on human lymphocytes cultured *in vitro,* with or without addition of phytohemagglutinin (PHA).

MATERIAL

Peripheral blood lymphocyte suspensions, purified in plastic containers (8), were incubated in TC 199 with 2% inactivated calf serum. The experiments were carried out in two series.

In the first series lymphocyte cultures without PHA were irradiated in two groups:

1. 4 h daily at 7 mW/cm^2 during 3 or 5 days.
2. 15 min daily at 20 mW/cm^2 during 3 or 5 days.

In the second series the effect of microwave exposure on PHA-transformed lymphocytes was examined, the experiments being carried out in the following groups:

1. Lymphocyte cultures following 66 h incubation were irradiated at 20 mW/cm^2 for 5, 10, 15, 20 minutes and 2 × 20 minutes with a 30 min interval.
2. Lymphocyte cultures following 64 h of incubation were irradiated 3 or 4 h at 7 mW/cm^2.
3. Lymphocyte cultures were exposed for 4 h daily during 3 days at 7 mW/cm^2.
4. Lymphocyte cultures were exposed to microwave irradiation for 10 min at various incubation periods: immediately after preparation of the culture (0 time) as well as following 59, 70 and 71.5 h of incubation.

METHODS

Lymphocyte cultures were exposed in a plastic thermostatic chamber (constant temperature of 37°C) at 7 mW/cm^2 or 20 mW/cm^2 to 2950 MHz pulsed microwaves (1200 Hz, 1 μs) using a horn antenna. Behind the exposure chamber an anechoic screen was placed, to avoid reflections and interference. The power density of the beam and the temperature of the incubation medium were controlled during each experiment.

The temperature of the medium remained constant during 4 h at 7 mW/cm², at 20 mW/cm² it increased after 15 minutes by 0.5°C. Prolonged irradiation at this power density caused after 20 minutes an increase by 1°C.

In all experiments of the second series 0.05 mg of colcemide per 1 ml medium was added following 66 h of incubation, and the cultures were harvested after 6 h from the moment of colcemide addition (hypotonia, acetic alcohol fixation, Giemsa stain of air-dried preparations).

RESULTS

Microwave exposure at 20 mW/cm² induced changes in the mitotic index which depended on the exposure time (Tab. 1). 5 min exposure did not influence the proportion of dividing cells, slight differences compared with controls were observed after 10 and 15 minute exposures, significant differences were seen following 20 and 40 min exposures. Similar results were obtained following 3 or 4 h exposure at 7 mW/cm² at periods later than the 64th hour of incubation. The mitotic index was approximately two times higher in irradiated samples than in control ones. This effect became noticeable in cultures irradiated during the 59th hour of incubation and was pronounced in cultures irradiated after the 64th hour of incubation (Tab. 2). Irradiation after 70 or 71.5 hrs of incubation influenced the miototic index only in a very slight degree. Exposure of lymphocytes at 20 mW/cm² for various periods of time induced changes in numbers and structure of chromosomes which depended on the duration of exposure (Tab. 3). Only slight differences from control samples were noted after a 5 min exposure, more pronounced changes were seen after longer exposures. Stickiness of chromosome arms (Fig. 1) and aneuploidy were observed. Hyperploidal cells up to 85 chromosomes were encountered. Figure 2 shows a hyperploidal (about 3 N) cell. Dicentrics (Fig. 3) and chromatid breaks (Fig. 4) were also seen. It should be pointed out that changes in chromosomal morphology suggesting changes in spiralization were the most unusal finding (Fig. 5) Similar pictures were observed in chromosomes of

Table 1

Percent of blastoid forms, lymphocytes and mitotic index in dependence from exposure time at 20 mW/cm²

Exposure time min	% Blastoid forms	% Lymphocytes	Mitotic index % (M. I.)	Expected range for M. I. at 95% confidence level
0	78.0	10.0	12.0	10—15
5	79.0	8.3	13.7	9—16
10	78.2	4.6	17.2	13—17
15	75.8	6.3	17.9	13—17
20	73.5	3.0	23.5	18—22
40 (2×20)	74.0	1.0	25.0	23—27

Table 2

Percent of blastoid forms, lymphocytes and mitotic index following 10 min exposure at 20 mW/cm^2 during various incubation periods

Hours of incubation	% Blastoid forms	% Lymphocytes	Mitotic index % (M. I.)	Expected range for M. I. at 95% confidence level
0	73.0	15.0	12.0	10—14
59	80.4	4.0	15.6	12—18
64	78.0	5.0	17.0	14—19
70	79.8	10.0	10.2	8—13
71.5	80.0	9.0	11.0	9—14
Control	81.1	9.4	9.5	8—13

Table 3

Dependence of chromosomal aberrations on exposure time, 20 mW/cm^2

Exposure time in min	Normal mitoses	Stickiness	Chromosomal aberrations			
			Dicentrics	Hypoploidy	Hyperploidy	Breaks
5	85.0	5.0	6.0	2.0	1.0	1.0
10	57.0	17.0	9.0	4.0	8.0	7.0
15	45.0	34.0	9.0	3.0	4.0	5.0
20	34.0	20.0	10.0	3.0	5.0	28.0
Control	92.0	2.0	4.0	0	0	2.0

irradiated rat kangaroo cells by Yao and Jiles (13). These authors call such changes "electromagnetic degeneration of chromosomes". Phagocytic forms containing nuclear fragments or phagocytized chromosomes were encountered. Moreover fragmentation of nuclei and nuclear vacuolization were seen. Certain pictures recalled cells in amitosis. Nuclear bridges were also not infrequent. The highest number of chromosomal aberrations was seen after exposure during the 70th hour of incubation. In this instance the number mitoses with chromosomal aberrations reached 50%.

The experiments demonstrated that microwave irradiation of PHA-stimulated human lymphocyte cultures at power densities of 7 mW/cm^2 and 20 mW/cm^2 causes an increase in the mitotic index as compared with control samples. A dependence between the value of the mitotic index and duration of exposure seems to exist. It should be stressed that irradiation of lymphocytes without PHA addition induces the appearance of blastoid forms and macrophage-like cells (Fig. 6).

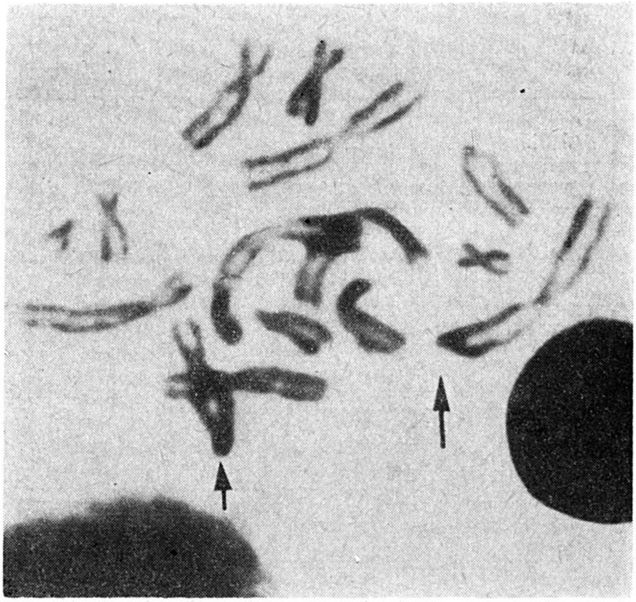

Fig. 1. Stickiness of chromosome arms.

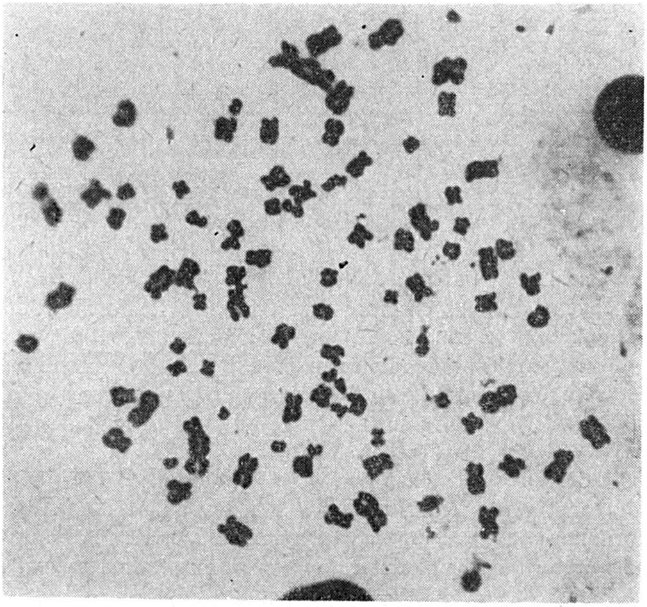

Fig. 2. A hyperploidal cell in a microwave-irradiated culture.

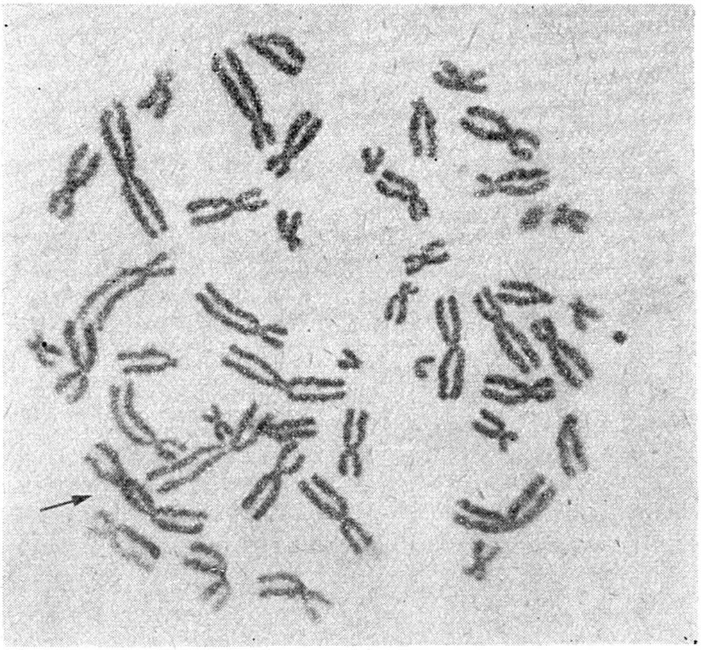

Fig. 3. A dicentric chromosome.

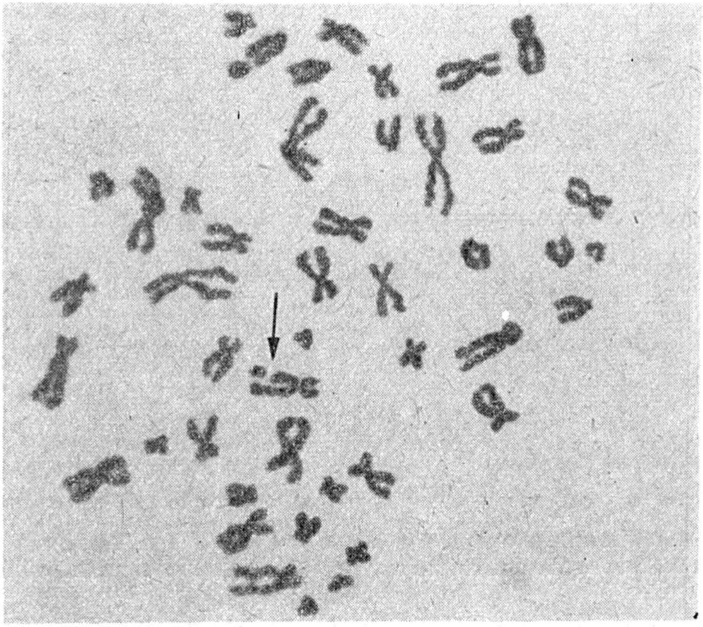

Fig. 4. Chromatid break.

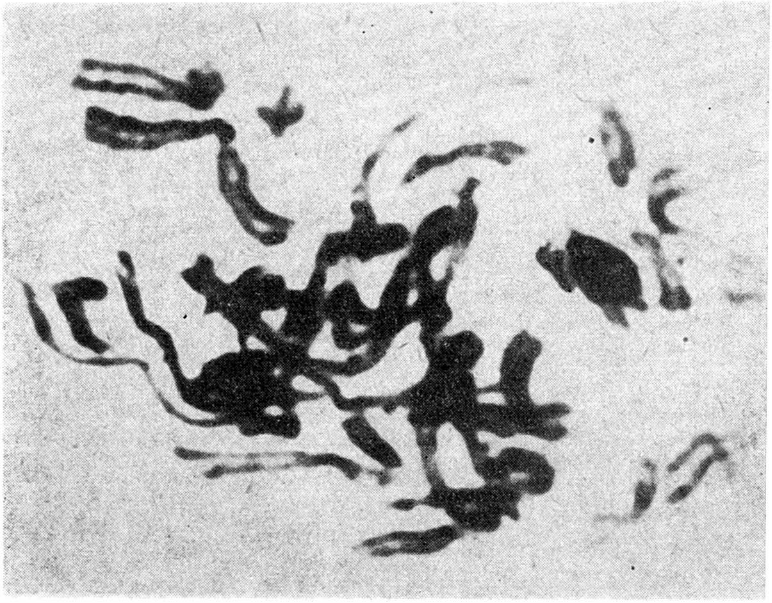

Fig. 5. Changes in chromosome spiralization.

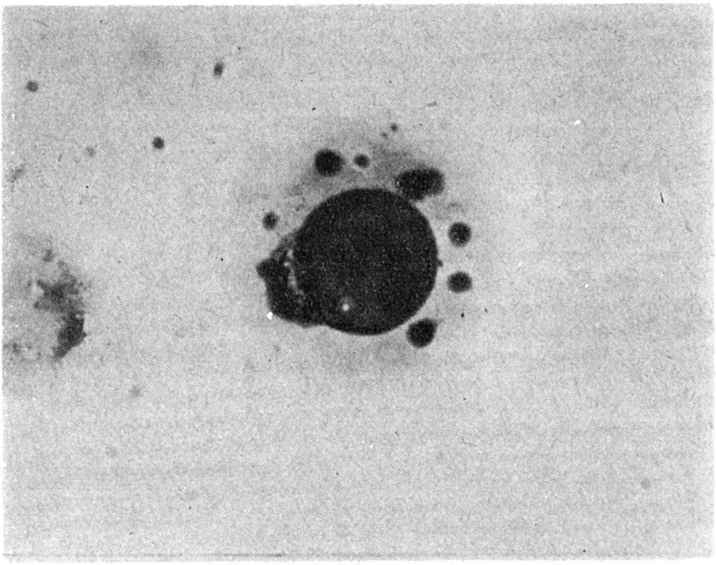

Fig. 6. A macrophage-like cell.

DISCUSSION

The presented above results suggest that microwaves may have mutagenic effects. Reports on point mutations in *Drosophila melanogaster* (10) strengthen this suspicion. The mechanism of blastic transformation and mitotic stimulation of lymphocytes by microwaves is unclear and should be investigated further. It seems worth mentioning that an increase in absolute lymphocyte counts in peripheral blood and stimulation of lymphocytopoiesis has been observed *in vivo* in animals following long-term, low-dose exposure (2, 3, 6, 7). Microwave-induced mitotic and chromosomal aberrations have been described in other types of cells in tissue culture (6, 10) and in plants.

The results obtained indicate also that microwave exposure may induce changes in interphasic nuclei. Irregular outlines of the nucleus in several instances suggested that fragments may be split off. It should be stressed that as far as we know microwaves are the only physical agent capable of inducing lymphoblastoid transformation (1). This seems to be interesting from a theoretical point of view. It is the author's feeling that this phenomenon could be used in investigations on the mechanism operative in blastic transformation of lymphocytes.

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MICROWAVE THAWING OF CELLS AND ORGANS

W. A. G. Voss, R. V. Rajotte and J. B. Dossetor

The Surgical Medical Research Institute, The University of Alberta, Edmonton, Alberta
Canada

INTRODUCTION

The use of energy in the microwave spectrum provides a method of controlling the rate and uniformity of heating of deep-frozen materials. If human organs are ever to be recovered from temperatures at which storage banks are a realistic possibility, microwave thawing techniques have to be considered. A study of the biologic effects of microwave heating on nucleated cells in the range from —196°C to +35°C is an essential step in the search for methods of viable organ preservation.

High survival rates for several cell types in tissue culture thawed by short wave diathermy (27 MHz) have been reported (8). Microwave and short wave (2450 and 27 MHz) thawing of canine kidneys have been briefly reported (3), but, so far, there have been no reports of the recovery of viability and function of deep-frozen kidneys, by any of the freezing and thawing regimes used.

Thawing of biological materials is conventionally achieved in a water bath. A high degree of success has been obtained with cells of many types and certain multicellular structures. Skin and cornea are preserved clinically in the frozen state (6, 9); in fact, an encouraging number of advances have recently been made in the preservation of other multicellular structures using water bath thawing. The cryobiological methods used have been described in a number of books (6, 9) and an excellent review of freezing phenomena has been given recently by Mazur (5). Whittingham, Leibo and Mazur (11) froze 2—8 cell mouse embryos to —196°C and —269°C at slow cooling rates (0.3 to 20°C/min) and then thawed slowly at rates of 4° to 25°C/min in a water bath, with subsequent success. The cryoprotective agent dimethyl sulfoxide (DMSO), at 1 M concentration, was about twice as effective as an equal concentration of glycerol. These particular compounds penetrate all membranes, reduce the free water content and thereby the damage from high concentrations of intra- and extracellular solutes that would otherwise be present at that temperature. Optimum cooling rates have been established in many cases.

Supercooled adult hearts have resumed beating but attempts to freeze adult mammalian hearts have met with only limited success. A detailed review of the subject has been given by Luyet (4). Other organs have withstood supercooling.

The small, fully differentiated heart also provides a convenient model for studying the effects of microwave thawing. Not only is it possible to determine the effects of the insult at different power levels, the method of controlled thawing may have immediate applications in, for example, the preservation of adult heart valves, the selective preservation of certain cells, improved preservation techniques for embryos in animal husbandry and eventually, help to determine whether or not the kidney, the organ in greatest transplant need, can be preserved indefinitely. The latter is probably the greatest challenge to preservation engineering today. It is not possible to describe the histologic, microfil, oxygen and para-amino-hippurate studies on frozen-thawed canine kidneys in detail in this paper, but the raw data and photographic information are available.

MICROWAVE HEATING SYSTEM DESIGN

In microwave biology studies, waveguide systems are preferable as the fields are known. Multimode cavities are unsatisfactory in this respect but in thawing applications, where the geometry of the material is often irregular, their use is indicated in many cases.

The two resonant microwave systems were cubic structures, the basic design following that of the conventional microwave oven. The smaller unit, a 10-inch cube, coupled to a 1 kW, 2450 MHz magnetron, was used for thawing tissue culture cells. A larger volume oven was required for thawing organs by our method: a 17-inch cube coupled to a 2 kW magnetron at the same frequency.

Both systems were equipped with rotating turntables on which the samples were placed. In the larger cavity, the Teflon turntable was oscillated as well as rotated, through a Teflon shaft powered from two independent external electric motors. This system is shown in Figure 1. The turntables and drive shafts were made of Teflon, a durable material which does not absorb microwave energy. When 2 ml or 5 ml samples (tissue culture cells and fetal hearts in different solutions) were heated *in vitro* a thermal insulating styrofoam cover was placed over the samples. Heating times were determined experimentally in advance; samples that were not recovered in the range 0 to 40°C were rejected. Heating rates were selected to be similar to those obtained in a water bath with 2 ml to 5 ml samples. Perfused, frozen kidneys were immersed in a 1 litre Teflon container filled with fluorocarbon, a material which was also used for the organ perfusate. Organs were frozen at 1°C/min by the method shown in Figure 2.

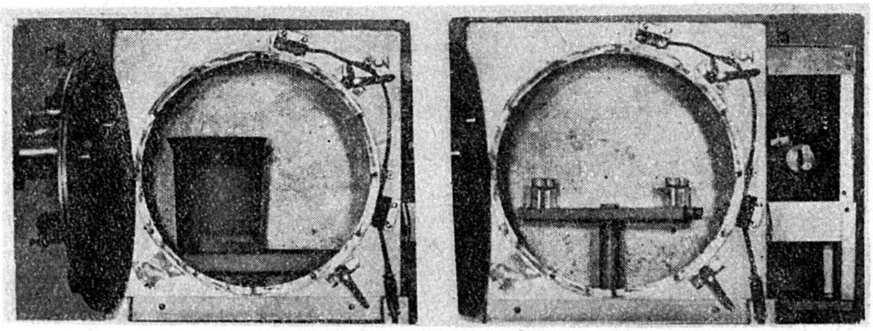

Fig. 1. Microwave thawing system. The two turntables are shown at the top through the open cavity door.

The 17-inch cubic cavity was used or thawing canine kidneys and fetal hearts, conditions representing very different degrees of loading. For thawing tissue culture cells, we were interested in applying very high field strengths, to determine the effect on their survival. The smaller cavity was used for this; in the absence of a load, corona discharge was detected around the Teflon shaft at 1 kW input power. Rotating two 2 ml samples in the oven, with a 50 ml water load in one corner of the cavity gave rise to a significant

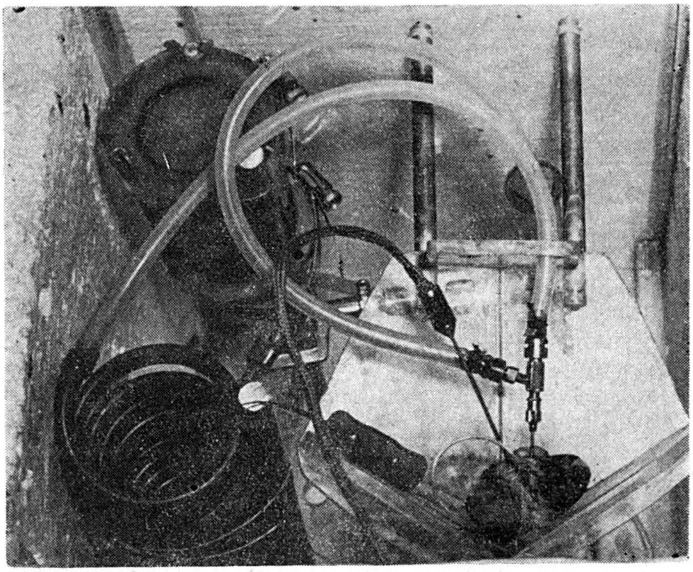

Fig. 2. Inside view of the freezing chamber. Thermocouples control the cooling rate through the liquid nitrogen jet on the perfusate cooling coil shown at the lower left.

preferential heating of these samples, at the same time reducing the reflected power back to the magnetron to about 50%. The electric field strengths in the cavity have not been measured but it is assumed that peak values are in the range 1000 to 10 000 volts/cm.

These systems lack refinement and the approach is entirely experimental. For our initial purposes the systems have worked, providing rapid uniform thawing and some basic data. In the work reported here using cavities we have operated at a mean heating rate which approximately corresponds to that obtained with 2 ml samples thawed in a 35°C water bath. However, the initial and final rates are quite different owing to the changing dielectric properties of the liquids and tissue. The mean absorbed power densities were of the order of 10 W/cm^3 in the majority of cases.

MICROWAVE THAWING OF TISSUE CULTURE CELLS

The results have been reported (30) and demonstrate very clearly that no disadvantages to microwave thawing procedures, with a cell system, are apparent if the final temperature is below about 10°C. Thus, the absorption of energy resulted in rapid and uniform thawing. Survival figures as good as, or better than, those realized with standard thawing procedures can be achieved for Chinese hamster cells. Twice the conventional thawing rate is acceptable and it is to be noted that, theoretically, this is relatively independent of sample shape and size. However, this statement must be qualified as the heating rates in different temperature ranges are quite different.

Microwave thawing of fetal mouse hearts

The fully differentiated fetal heart of the mouse can be reimplanted in the ear of an adult syngeneic mouse and studied electrically over a long period of time. Immunologically, this is equivalent to transplantation between identical twins in man. Microwave energy (at 2450 MHz) was used as one method of thawing and compared to thawing in a water bath.

Materials and methods

Heart transplant. Hearts were removed from Balb-c fetuses obtained at 16—18 days gestation. The hearts at this time measure approximately 1 mm in diameter and beat rhythmically. Following thawing, the embryonic hearts were implanted directly into the ear of adult syngeneic mice anesthetized by Nembutal. The anterior aspect of the ear was injected subcutaneously with 0.1 ml of saline. The injection causes the two layers of skin to separate and thus form a pocket for the fetal heart. A small incision was made to introduce the fetal heart into the subcutaneous space. Fetal hearts implanted in this manner are nourished by the surrounding tissue fluid until an abundant capillary supply is formed some days after grafting (2).

Freezing. The fetal hearts were placed in prechilled solutions: Eagle's minimal essential medium (MEM) containing Hepes buffer, 10% (v/v) fetal calf serum and 10% (v/v) dimethyl sulfoxide (DMSO) or McCoy's 5a medium containing Hepes buffer, 10% (v/v) fetal calf serum and 10% (v/v) DMSO were successful. The DMSO was added slowly. The freezing rate was maintained between 0.5 and 0.7°C/min, by a thermocouple control system, down to —100°C. The samples were then placed in liquid nitrogen vapor and cooled at 5—10°C/min down to —196°C. They were stored for 72—216 h at —196°C before being rewarmed.

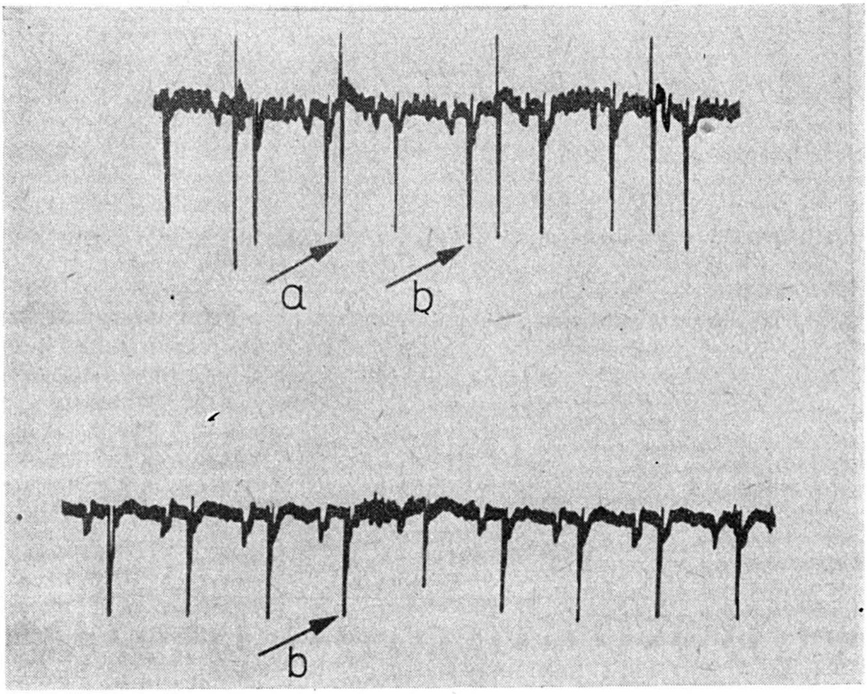

Fig. 3. A typical ECG showing normal mouse complexes (arrow b) at approximately 250 beats/min with the slower superimposed fetal heart rhythm (arrow a).

Thawing process. Frozen hearts were rewarmed either by placing the 5 ml vials in a 35°C water bath, thereby raising the temperature at a rate of ∾ 150°C/min or in the microwave system described. In these experiments, mean heating rates of 200°C/ /min were used to thaw the hearts from —196°C to 20°C ± 10°C.

Assay of graft function. It is not possible to assess the pump action of the graft; however, the electrical property was evaluated by electrocardiography and contractility could be seen with a magnifying glass through the skin of the external ear. The adult heart function (b) and that of the fetal heart (a) can be recorded simultaneously as two distinct sets of rhythmic electrical activities, Figure 3.

Results

As controls, Balb-c mice received direct syngeneic ear transplants of unfrozen fetal hearts. 95% of these control transplants had electrical activity by the 5th day and continued to function for periods in excess of 90 days. 18 out of 30 hearts thawed by microwaves and 14 out of 20 thawed in the water bath showed similar overall biphase electrical activity after 35 days.

From these results, it is concluded (a) that both DMSO and fetal calf serum may encourages the hope that it may be effective with larger tissues where water bath thaw-injury, (b) that microwave thawing is as effective as thawing in a water bath, which encourages the hope that it may be effective with larger tissues where water bath thawing would certainly be ineffective, and (c) that this model can be used, in future work, to assess different cryoprotective agents and freeze-thawing techniques on survival of a multicellular organ which is at the upper limit of size for nutritional survival by diffusion and neo-capillary ingrowth, i.e. the upper limit of size for survival without the need for direct vascular anastomosis at the time of graft implantation.

MICROWAVE THAWING OF KIDNEYS

In attempting to design a complete freeze-thaw system, our objective has been to use the most promising perfusates in a system which allows for the controlled variation of the basic parameters, uniform freezing and thawing rates. If controlled, uniform freezing and thawing cannot be obtained, there seems little purpose in other experiments on whole organ preservation.

The freezing system, shown in Figure 2 is rate controlled by the thermocouples to ± 5°C variation. Fluorocarbon was chosen for subsequent perfusion at temperatures below +4°C as it is biologically and physicochemically acceptable, and will perfuse through the critical tissue freezing range (—15 to —40°C) without requiring abnormally high perfusion pressures. At about —40°C, environmental cooling was then used down to —79°C at the same rate. For thawing, the frozen kidneys were placed individually in a Teflon holder. After thawing, kidneys were perfused with Ringer's lactate containing either 10% DMSO or 10% mannitol initially and then Ringer's lactate by itself.

Results

A group of kidneys which were not frozen but had been permeated with the protective agent, followed by perfusion at 4°C with FC47 and warmed in the microwave system, showed what was judged to be near normal histology and assessed as 'viable' after anastomosis via the femoral artery in the vein of the same dog for a number of hours. The histology of microfil injection indicated a normal kidney.

Some kidneys thawed from —79°C at rates between 100 and 200°C/min showed satisfactory temperature profiles if the perfusion was complete. Overheating of the external ureter was seen in several kidneys. A kidney reimplanted in the groin of the same dog after a complete freeze-thaw cycle, was examined after 5 days. Although the external appearance was completely normal, damage to the microcirculation was subsequently apparent. In isolated areas glomeruli and capillaries were well preserved indicating that the blood was being perfused through the organ. Other parts of the kidney showed gross damage, and, in fact, could not be properly injected with microfil. At no time was there evidence that the kidney was capable of forming urine.

Our histological studies, with microfil sections and thawing profiles, have clearly demonstrated the difficulty in assaying damage due to the freeze-thaw insults, in line with the experiences of Abbott (1). So far however we have no definite reason to reject microwave thawing at the organ level. The fact that some nucleated cells and one very small multicellular organ will survive a series of gross insults of this type is encouraging.

ACKNOWLEDGEMENTS

We wish to thank all the members of the MRC Transplantation Group and the Surgical Medical Research Institute at the University of Alberta for their contributions to this continuing work. We express our gratitude also to the Medical Research Council of Canada and the National Research Council of Canada for their financial support of this work.

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Session D. Measurements of Microwave Radiation

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QUANTITATION OF INDUCED ELECTROMAGNETIC FIELD PATTERNS IN TISSUE AND ASSOCIATED BIOLOGIC EFFECTS

A. W. Guy

Department of Rehabilitation Medicine, University of Washington, School of Medicine, Seattle, Washington, U. S. A.

INTRODUCTION

It is the desire of both the users and those who regulate the use of electromagnetic (EM) power to promulgate exposure guides that are conservative enough to insure the safety of man but do not unnecessarily restrict the application of the energy for the benefit of man. Such guides must be based on a quantitative understanding of the relationship between any biologic effect or damage, the fields induced in the affected tissue, and the fields in the environment of the exposed subject. In order to properly evaluate the hazard, it is also necessary to determine whether an observed effect is due to indirect thermal action, or whether it is directly related to the fields induced in the subject. Thus, a quantitative description of the EM fields within the tissues and an understanding of the relationship between these fields and the thermodynamics of the biologic system are desirable. The latter also provides a basis for useful instrumentation techniques for determining absorbed power densities and induced fields in the tissues of the exposed subjects by simple temperature measurements.

THERMAL CONSIDERATIONS

The energy equation for the time rate of change of temperature (°C sec) per unit volume of subcutaneous tissue in a subject exposed to EM fields is $dT/dt = 0.239 \times 10^{-3}/c\ [W_a + W_m - W_c - W_b]$ where W_a is the absorbed power density, W_m is the metabolic heating rate, W_c is the heat loss due to thermal conduction, W_b is the power dissipated by blood flow, all expressed in W/kg, and c is the thermal conductivity expressed in kcal/kg $-$°C. The absorbed power density for tissue exposed to an EM field is $W_a = 10^{-3}\sigma/\varrho E^2$ where σ is the electrical conductivity in mhos/meter, ϱ is the tissue density in g/cm^3, and E is the rms value of the electric field (V/m) in the tissue. If it is assumed that blood enters the tissue at arterial temperature T_a and leaves at tissue temperature T, we may express blood cooling by $W_b = k_2 m c_b/\varrho_b \Delta T'$ where $\Delta T' = T - T_a$, c_b is the specific heat of blood, ϱ_b is the density of blood, m is the blood flow rate in ml/100 g-min, and the constant $k_2 = 0.698$. Prior to the time the tissue is exposed to fields, it is assumed that a steady state condition exists where $W_a = dT/dt = 0$ requiring $W_m = W_c + W_b$. According to the typical values of the physical and thermal properties of tissues given in Table 1, under normal conditions the metabolic rate W_m averages 1.3 W/kg for the total body, 11 W/kg for brain tissue, and 33 W/kg for heart tissue. According to the energy equation, we would expect to see some change in tissue temperature due to applied EM fields if the power absorption density W_a were of the same order of magnitude as W_m or more. In fact, the safety guides in the United States that allow a maximum human exposure level of 10 mW/cm^2 of incident power are partially based on limiting the average W_a to the average resting value of W_m. Thus, absorbed power densities $W_a >> W_m$ could be expected to produce marked thermal effects, whereas power densities $W_a << W_m$ would not be expected to produce any significant thermal effects. Safety guides, how-

Table 1

Thermal and physical properties of human tissues

Tissue	Subscript	Specific heat (c) kcal/kg	Density σ(1) g/cm^3	Metabolic rate (W_0) W/kg	Blood flow rate (m) ml/100 g · min	Thermal conductivity (k_c) kcal/kg− °C
skeletal muscle (excised)	m	0.83	1.07			4.4
skeletal muscle (living)	m			0.7	2.7	6.42
fat	f	0.54	0.937			2.1(1)
bone (cortical)	bc	0.3	1.79			14.6(1)
bone (spongy)	bs	0.71	1.25			
blood	bl	0.93	1.06(2)			5.06
heart muscle	m			33	84	
brain (excised)						5.0
brain (living)	br			11	54	8.05
kidney	k			20	420	
liver	l			6.7	57.7	
skin (excised)	s					2.5
skin (living)				1	12.8	4.42
whole body				1.3	8.6	

(1) For pig
(2) For humans

ever, are not, and cannot be, specified in terms of absorbed power density, but are more conveniently expressed for radiation fields in terms of an incident power flux density expressed in units of mW/cm^2 or, for the case of stationary or quasi-stationary fields, they may be expressed in terms of electric field strength E, in V/m, or magnetic field strength H, in a/m. The latter two quantities can also be expressed in terms of stored energy density, $\varepsilon_0 E^2$ or $\mu_0 H^2$, where ε_0 is the permittivity and μ_0 is the permeability of free space. It is virtually impossible, however, to classify any of the above field quantities measured exterior to an exposed subject as being hazardous, non-hazardous, thermal, or non-thermal, without first knowing enough about exposure conditions, frequency, subject size, and subject geometry to determine what the absorbed power density in the subject actually is. Peak values of absorbed power density 50 W/kg $\leq W_a \leq$ 170 W/kg have been used to provide vigorous therapeutic heating of deep vasculated tissues in man treated with diathermy (4), and values of $W_a \geq$ 4 W/kg absorbed in brain tissue of cats provided measureable increases in brain temperature and decreases in latency times of evoked potentials (6). Body temperature increases, accompanied by behavioral changes, have been observed in rats by Justesen (7), for $W_a \geq$ 3.1 W/kg, and by Hunt et al. (5), for $W_a \geq$ 6.3 W/kg, averaged over the body of the animal. Changes in body temperature, thermoregulatory, cardiovascular, and metabolic characteristics were observed by Philips et al., (10) for rats exposed to fields such that W_a = 6.3 W/kg averaged over the body of the animal. Cataracts have been induced in rabbits by acute exposures where power absorption density in the eye was greater than 138 W/kg accompanied by marked increases in temperature (8).

FORCE EFFECTS

In addition to tissue heating, electromagnetic energy can produce forces at the surface of an exposed subject, forces across internal tissue, or cell interfaces, and pressure changes in body fluids proportional to E^2. Schwan (12) has shown that one such effect, pearl chain formation of suspended particles in a fluid, can only occur in a biologic medium at field levels that are also thermally damaging. Both thermal effects and pearl chain formation, which depends on a sustained force, are related to average power absorption and do not relate to the peak absorbed power from modulated or pulsed EM fields. On the other hand, the evoked auditory effects in man and animals appear to be related to the instantaneous value of pulsed fields at average field levels that are far below those capable of producing temperature changes in the tissues. Frey (1) has found the loudness of the effect in humans to be proportional to peak power for pulse widths greater than 60, whereas Guy et al. (2) have found the threshold for the evoked responses in humans and cats to be related to the energy per pulse (20 to 40 μJ/cm^2 incident energy density or of the order of 15 mJ/kg absorbed energy) for pulse widths from 1 to 30 μs, regardless of average and peak power. Whether these effects are due to impulsive field forces or some other unexplained interaction has not been determined.

RELATIONS BETWEEN INCIDENT FIELDS AND POWER ABSORPTION DENSITY

Considerable insight can be gained into the relationship between frequency, body size, and absorbed power by considering spherical tissue layers exposed to a plane electromagnetic wave. Figure 1 illustrates the relative absorbed power density patterns

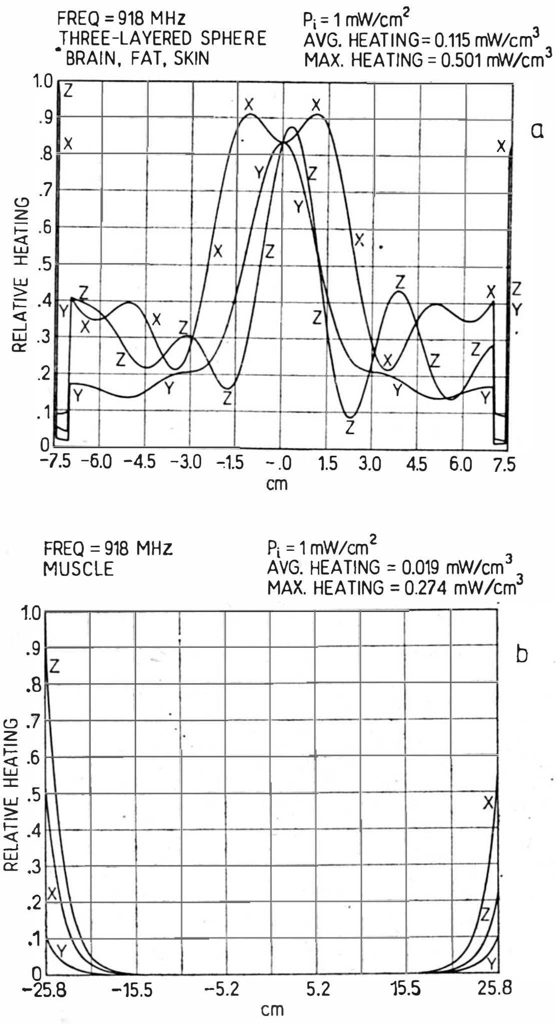

Fig. 1. Power absorption densities in spherical tissue layers exposed to 1 mW/cm^2 incident plane wave power density. a. Spherical model of human head with brain core surrounded by thin layers of bone and skin exposed to 918 MHz radiation (radius in the order af a wavelength in tissue). b. Spherical homogenous muscle model simulating man exposed to 918 MHz radiation (radius large compared with a wavelength with tissue).

for various spherical tissue geometries exposed to a 1 mW/cm^2 plane wave source. The origin of the rectangular coordinate system used in the figures is located at the center of the sphere with wave propagation along the z axis and the E field polarized along the x axis. The maximum absorption and the average absorption density are tabulated on each plot. When the diameter of the exposed object is of the order of one wavelength as measured in the tissue, severe internal wave interference produces sharp maxima and minima in the power absorption patterns as shown in Figure 1a for a sphere representing a human head exposed to 918 MHz radiation. The spherical model is composed of an inner core consisting of brain tissue surrounded by a layer of bone and skin.

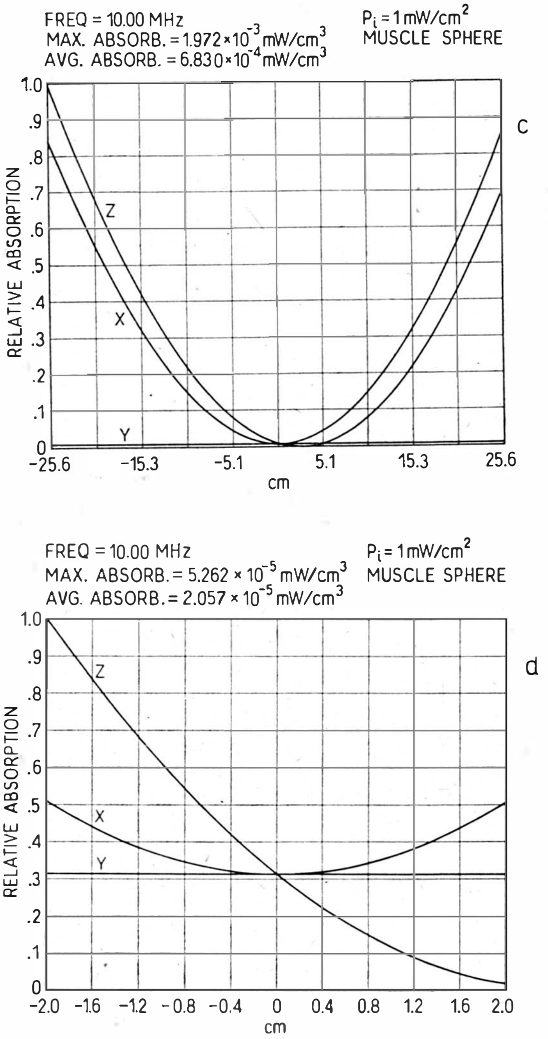

Fig. 1. c. Spherical homogeneous muscle model simulating man exposed to 10 MHz radiation (radius small compared with a wavelength in tissue). d. Spherical homogenous muscle model simulating a mouse exposed to 10 MHz radiation (radius small compared with a wavelength in tissue).

When the object is large compared with a wavelength, as measured in the tissue, the maximum absorption occurs at the exposed surface, decaying nearly exponentially with depth as shown in Figure 1b for a homogeneous muscle sphere with the same mass as a 70 kg man exposed to 918 MHz radiation. When the exposed subject is very small compared with a wavelength, but of a mass approximating that of man, the power absorption density varies nearly as the square of distance from the y axis (direction of magnetic field vector) as shown in Figure 1c. On the other hand, if the object is very small compared with a wavelength, but with a small mass, the power absorption density is uniform along the y axis but increases with distance toward the exposed surface and

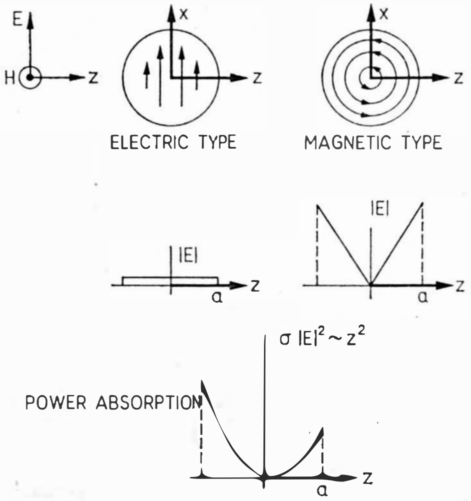
E
H
Z
X
ELECTRIC TYPE
MAGNETIC TYPE
|E|
a
σ |E|² ~ z²
POWER ABSORPTION

Fig. 2. Sketch depicting how electric and magnetically induced electric fields add in exposed tissue sphere to produce absorbed power distribution pattern.

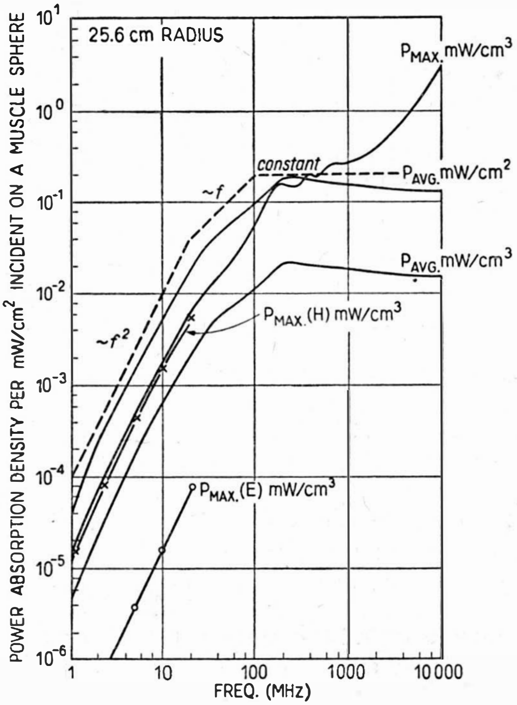

Fig. 3. Power absorption density patterns versus frequency in spherical muscle model of 70 kg man exposed to plane wave 1 mW/cm² source.

decreases with distance toward the opposite surface, as shown in Figure 1 d. The latter two absorption patterns for objects small compared with a wavelength can be explained from simple quasistatic field theory (9). The electric field component of the incident plane wave couples to the object in the same manner as a static electric field giving rise to a constant internal electric field which is $3/\varepsilon$ times smaller, and in the same direction as the applied field, where $\varepsilon \gg 1$ is the dielectric constant of the tissue. Superimposed on the constant internal electric field is another magnetically induced electric field component encircling the y axis as shown in Figure 2. The magnitude of the latter field, which varies directly with radial distance r from the axis, and directly with frequency f, is given by $E = \pi f r H$, where H is the magnetic field. The H-induced E field component in a man-size sphere is much greater than the E-induced component, whereas, for a small mouse-size object both components are significant. The variation of the maximum and average power absorption density with frequency for an exposed homogeneous muscle sphere with the same volume is shown in Figure 3. Also shown in the figure is the average power absorption density per unit total surface area of the sphere. In the frequency range from 1 MHz to 20 MHz, the absorption characterized by the pattern in Figure 2 c varies as the square of the frequency. This is due primarily to the magnetically induced fields. The maximum power absorption density induced by the incident H field is denoted by the curve marked with crosses, and that due to the incident E field is denoted by the curve with zeros in the range where the quasistatic coupling approximations apply. Note that in this range, the maximum power absorption density is only 10^{-5} to 10^{-2} W/kg per mW/cm^2 of incident power. In the frequency range 100 to 1000 MHz, internal reflections are significant for the man-size sphere and the average absorption attains a maximum of 2×10^{-2} W/kg per mW/cm^2 of incident power at 200 MHz, which remains relatively constant with frequency up to 10 GHz. The maximum absorption density increases with frequency above 1000 MHz, approaching that produced by non-penetrating radiation. The dashed lines illustrate roughly the frequency dependence of the total or average absorbed power and how safety standards might be relaxed as a function of frequency if the absorption charac-

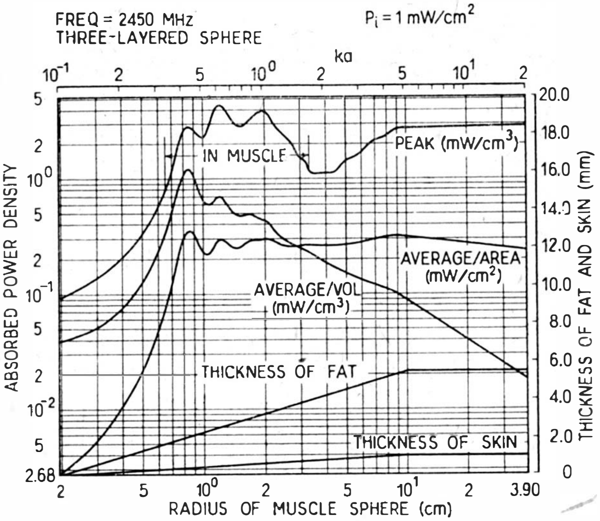

Fig. 4. Power absorption density versus outside radius in spherical tissue layer model of animal exposed to 2450 MHz 1 mW/cm^2 plane wave.

teristics in man were the same as for the sphere. The wide variation of absorption characteristics with body size is illustrated in Figure 4 for a sphere consisting of an inner muscle core surrounded by concentric layers of subcutaneous fat and skin exposed to 2450 MHz plane wave 1 mW/cm^2 radiation. The total radius, fat thickness and skin thickness are noted on the figure. It is significant to note that based on the spherical models, the peak power absorption could be as high as 4.2 W/kg in the body or head of a small bird or animal but as low as 0.27 W/kg at the surface, and 0.05 W/kg 2.5 cm deep in the human body exposed to a 1 mW/cm^2, 918 MHz source (Figure 1b). Thus, 10 mW/cm^2 could be of extreme and 0.5 mW/cm^2 could be of mild thermal significance to the smaller animal in comparison with metabolic rate. For the human model, on the other hand, 10 mW/cm^2 would appear to be of mild thermal significance and 0.5 mW/cm^2 would have negligible thermal significance.

MEASUREMENT OF ABSORBED POWER DENSITY

Though the sphere analysis provides some insight into the size and frequency dependence of absorption characteristics of the subject, it is not a substitute for quantifying the actual absorption in irregular body shapes. Electromagnetic fields or quantities related to the fields can be measured both *in situ* and *in vivo* in test animals or even humans by means of implanted microwave diodes, thermocouples, and thermistors. Thermocouples and thermistors were used extensively in the past for measuring the temperature rise in tissues exposed to radiation. There are several problems associated with the use of thermocouples or thermistors to ascertain absorbed power: 1) the element senses only the temperature of the tissue which is also a function of other mechanisms such as thermal diffusion, blood flow, and the thermoregulatory characteristics of the animal; 2) if the sensor is left in the tissue during irradiation, it can be directly heated by the RF fields or it can significantly modify the fields and the associated temperature rises; and 3) the sensor is relatively insensitive to low power densities.

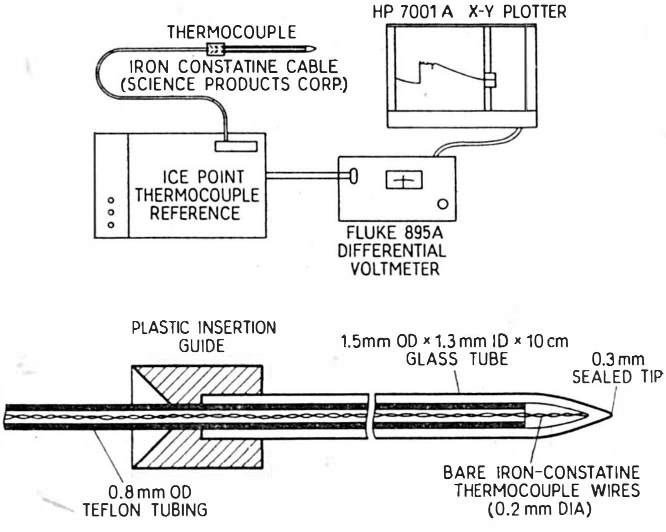
HP 7001 A X-Y PLOTTER
THERMOCOUPLE
IRON CONSTATINE CABLE (SCIENCE PRODUCTS CORP.)
ICE POINT THERMOCOUPLE REFERENCE
FLUKE 895A DIFFERENTIAL VOLTMETER
PLASTIC INSERTION GUIDE
1.5mm OD × 1.3 mm ID × 10 cm GLASS TUBE
0.3 mm SEALED TIP
BARE IRON-CONSTATINE THERMOCOUPLE WIRES (0.2 mm DIA)
0.8 mm OD TEFLON TUBING

Fig. 5. Apparatus used for determining power absorption density in biological tissue by a thermocouple.

All of these problems can be eliminated through a technique that utilizes a small diameter plastic or glass tube sealed at one end and implanted at the location where a measurement of the absorbed power is desired. The tube, illustrated in Figure 5, is long enough so that the open end, fitted with a plastic guide, protrudes from the tissue. A very small diameter thermocouple is inserted into the tube with the sensor located at the probe tip and an initial temperature is recorded. The thermocouple is quickly withdrawn from the tube and the animal is exposed under the normal conditions of the experimental protocol with the following exceptions. Instead of using the power level normally chosen for a given experiment, a very high power burst of radiation of duration sufficient to produce a rapid but safe temperature rise in the tissue is applied to the animal. The thermocouple is then rapidly returned to its original position and the new temperature is recorded for several minutes. The temperature versus time curve is then extrapolated back in time to the period when the power was applied and, based on the density and specific heat of the tissue, the absorbed power density is calculated from the difference between initial and final extrapolated temperatures. The short exposure period insures that there is no loss of heat due to cooling or diffusion, so integration of the energy equation over the short time period t gives $W_a = 4.186 \times 10^3\, c\Delta T/t$ where c is the specific heat of the tissue, ΔT the temperature change in degrees Celsius, and t the time of exposure in seconds. The measured absorbed power can then be used to relate the input power of the source to the absorbed power in the tissue under normal lower power exposure conditions. Figure 6 illustrates the measured absorbed power density in the eyes of rabbits exposed to the near zone field of a 2450 MHz diathermy applicator measured by this technique. The results have been used to establish the relationship between internal absorbed power and cataractogenesis (6). Guy (3), (6), has described a method for rapid evaluation of absorbed power density in tissues of arbitrary shape and characteristics when they are exposed to various sources, including plane wave, aperture, slot, and dipoles. The method, valid for both far- and near-zone fields, involves the use of a thermograph camera for recording temperature distributions produced by energy absorption in phantom models of the tissue structures. The absorbed power or magnitude of the electric field may then be obtained anywhere on the model as a function of the square root of the magnitude of the calculated heating pattern. The phantoms are composed of materials with dielectric

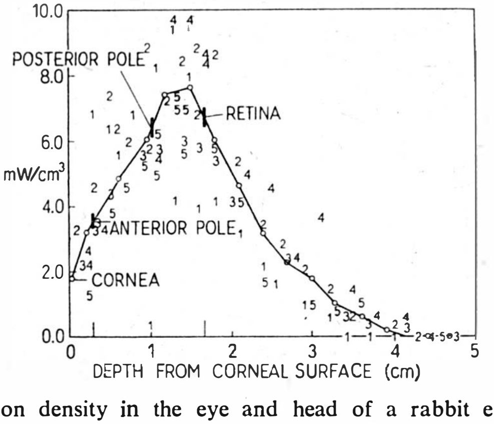

Fig. 6. Power absorption density in the eye and head of a rabbit exposed to 2450 MHz diathermy "O" director measured by a thermocouple method (values normalized to 1 watt input to applicator or 8.42 mW/cm^2 incident). Solid line is the mean of 5 rabbits.

and geometric properties identical to the tissue structures they represent. Phantom materials have been developed which simulate human fat, muscle, brain, and bones. These materials have complex dielectric properties that closely resemble the properties of human tissues reported by Schwan (11). The modeling material for fat may also be used for bone. The synthetic muscle can also be used to simulate other tissues with high water content. A simulated tissue structure composed of these modeling materials will have the same internal field distribution and relative heating functions in the presence of an electromagnetic source as the actual tissue structure. Phantom models of various tissue geometries can be fabricated as shown in Figure 7. They include circular cylindrical structures consisting of synthetic fat, muscle, and bone, and spheres of synthetic brain to simulate various parts of the anatomy. The models are designed to separate along planes perpendicular to the tissue interfaces so that cross-sectional relative heating patterns can be measured with a thermograph. A thin (0.0025 cm thick) polyethylene film is placed over the precut surface on each half of the model to prevent evaporation of the wet synthetic tissue. In using the model, it is first exposed to the same source that will be used to expose actual tissue. The power used on the model will be considerably greater, however, in order to heat it in the shortest possible time. After a short exposure, the model is quickly disassembled and the temperature pattern over the surface of separation is observed and recorded by means of a thermograph. The exposure is applied over a 5- to 60-s time interval depending on the source. After a 3- to 5-s delay for separating the two halves of the model, the recording is done within a 5-s time interval, or less. Since the thermal conductivity of the model is low, the difference in measured temperature distribution before and after heating will closely approximate the heating distribution over the flat surface except in regions of high temperature gradient where errors may occur due to appreciable diffusion of heat. The thermograph technique described for use with phantom models can be used on test animals. The animal under test or a different animal of the same species, size, and

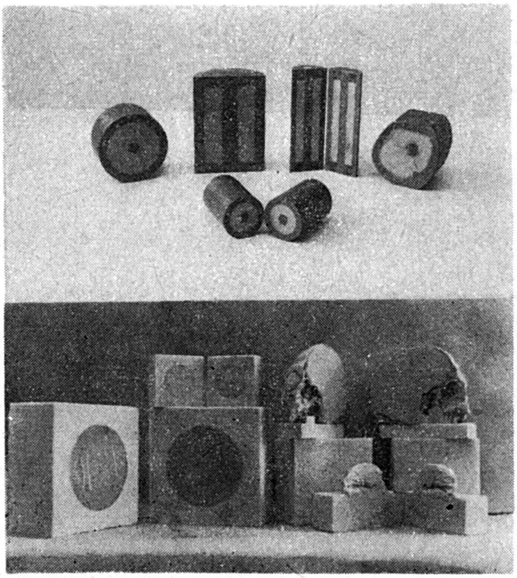

Fig. 7. Phantom tissue models.

characteristics must be sacrificed, however. The sacrificed animal is frozen with dry ice in the same position used for exposure conditions. It is then cast in a block of polyfoam and bisected in a plane parallel to the applied source of radiation used during the experiment. Each half of the animal is then covered with a plastic film and the bisected body is returned to room temperature. The same procedure used on the phantom model is then used with the reassembled animal to obtain absorbed power patterns over the two-dimensional internal surface of the bisected animal. Figure 8 illustrates thermographic recordings taken to assess the absorbed power density in an actual cat head and a 6 cm diameter phantom model of a head. The thermograms at the left of the figure are "C" scans taken over the surface of the separated hemispheres where brightness is proportional to absorbed power and each division is equivalent to 2 cm. The thermograms at the right of the figure are "B" scans taken before and after exposure where spacing between the curves is proportional to absorbed power as a function of vertical distance through the center of each subject. The results clearly show the presence of high absorption areas or "hot spots" in the head of the exposed cat predicted from the theoretical calculations for a sphere. Figure 9 illustrates a thermo-

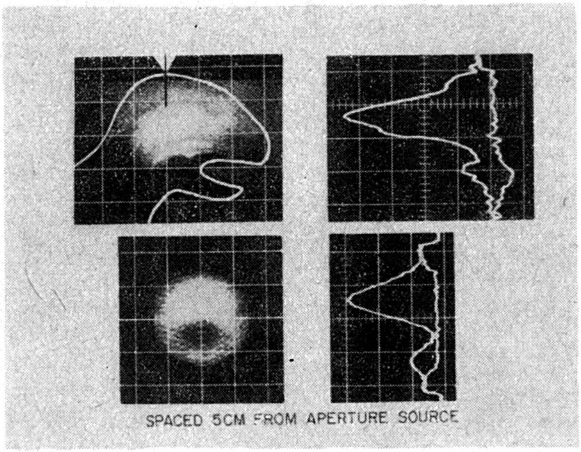

Fig. 8. Comparison between power absorption in cat head and 6 cm diameter phantom sphere (brain tissue) exposed to 918 MHz aperture source as measured with thermograph (peak absorption approximately 0.8 W/kg per mW/cm^2 incident power).

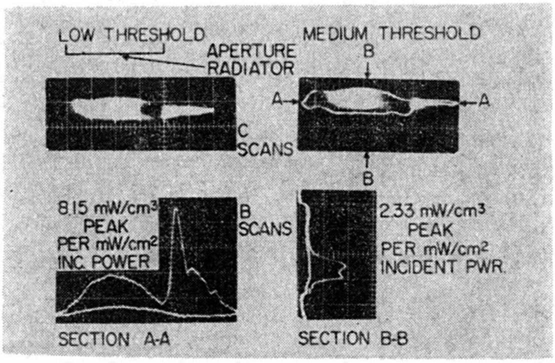

Fig. 9. Thermograms of phantom rat exposed to 918 MHz square aperture source.

graph study made on a phantom tissue model of the body of a rat exposed to a 918 MHz 13 × 13 cm aperture source outlined in the figure. The results clearly illustrate unpredictable absorption peaks (per mW/cm² of incident power) that may occur in the body and tail of the rat. The profound absorption (8.6 mW/cm²) at the base of the tail is due to the increased current density resulting from the sharp change in tissue cross-section. The low absorption in the pelvic area is due to a standing wave null resulting from a body resonance condition, since the rat model is approximately one wavelength long. The results indicate that one must be extremely careful in drawing conclusions from temperature measurements made with rectal thermometers. Also, one cannot make the easy assumption that keeping the tail or any portion of the rat out of the direct beam of radiation will insure non-exposure, and consequently, no absorption. The thermographic technique may be used to detect potential trouble from the use of metal electrodes or thermocouples in exposed biological tissues. Any metal object placed in tissue can result in serious field distortion and concentration in areas where the object is placed. Figure 10 illustrates thermograms taken of an exposed cat head with and without the presence of a standard coaxial metal electrode used for neurophysiological recordings. The results show a complete shift in the power absorption pattern and two orders of magnitude increase in the absorbed power density in the region where the tip of the probe is located. The past use of such electrodes in assessing the biological effects of microwave radiation on the CNS could result in the interpretation of highly localized thermal effects as non-thermal or low-level effects.

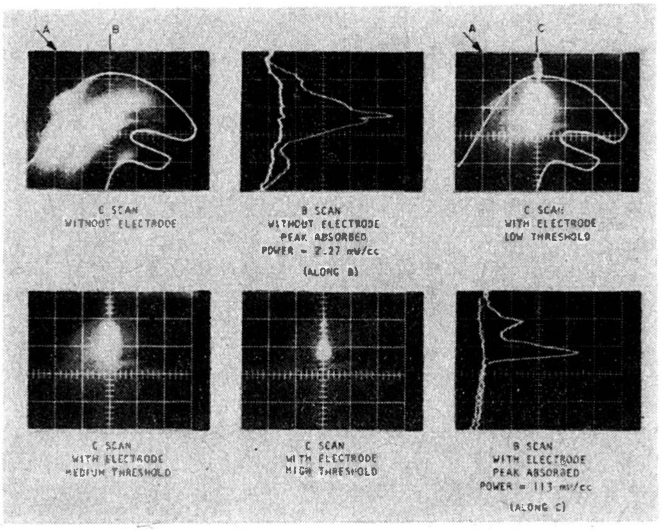

Fig. 10. Thermographic study of effect of coaxial electrode on microwave absorption pattern in the brain of a cat exposed to 918 MHz aperture source (incident power density = 2.5 mW/cm² scale, 1 division = 2 cm).

LABORATORY PROTOCOL FOR QUANTIFYING CNS EFFECTS OF EM RADIATION

It is important that any experimental protocol used to quantify absorbed power and associated effects in an animal be carefully planned to eliminate the possibility of misinterpreted data for the various reasons described above. Figure 11 illustrates an experimental protocol used by the author for assessing microwave induced CNS effects. Anesthetized cats are placed in a standard stereotaxic head holder, but the metal ear, orbit, and tooth bars are replaced by plastic parts to eliminate any metallic contact with the cat. The fields are applied to the head with a variable power localized source. The response of the thalamic somatosensory area of the cat's brain to electrical stimulation of the skin on the contralateral forepaw was recorded both with and without the presence of microwave radiation. The gross thalamic electrical response was detected by means of a saline-filled glass electrode with a 60-μm-diameter tip. The electrode was placed in the thalamus and adjusted for optimum thalamic response. The electrode's position was verified in several animals by histologic studies. Metal electrodes were avoided to prevent perturbation of the microwave fields in the brain tissue. The electrode and associated reference electrodes were coupled to lowpass microwave filters by a pair of 1-mil-diameter[1] high-resistance wires. The filter was designed to provide more than 150-dB attenuation to the microwave with no more than 20 pF of shunt capacitance to the input of a pair of field-effect transistors. The output of the transistors was fed through a processing differential amplifier to an analog tape recorder and computer of average transients. The body temperature of the cat was held constant by a heating pad connected to a rectal temperature control unit. The brain temperature was recorded during the time that the microwaves were off by placing a thermocouple in

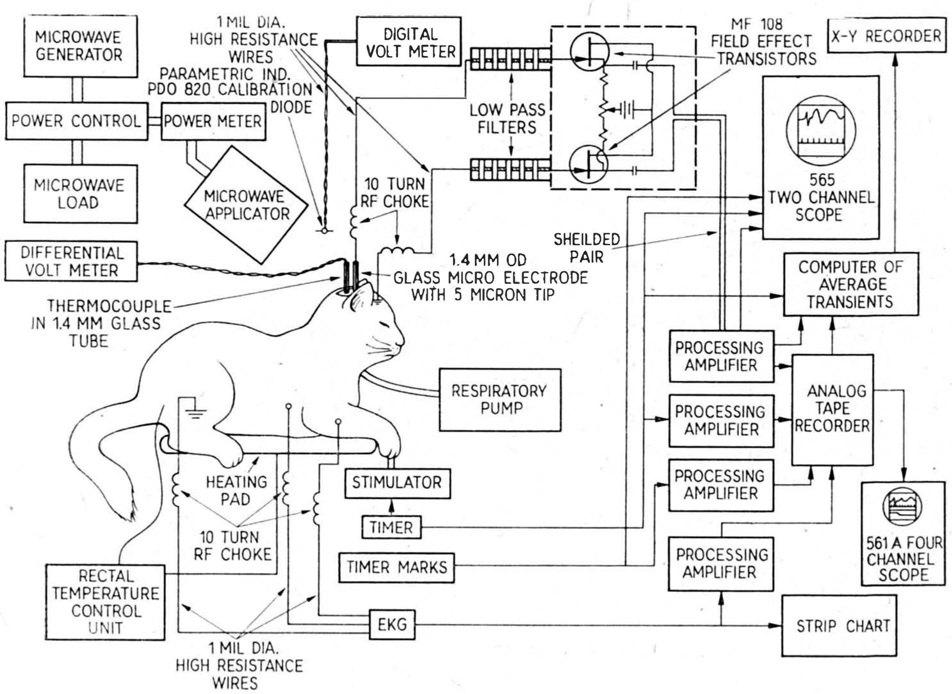
MICROWAVE GENERATOR
1 MIL DIA. HIGH RESISTANCE WIRES
DIGITAL VOLT METER
MF 108 FIELD EFFECT TRANSISTORS
X-Y RECORDER
PARAMETRIC IND. PDO 820 CALIBRATION DIODE
POWER CONTROL
POWER METER
LOW PASS FILTERS
MICROWAVE LOAD
MICROWAVE APPLICATOR
10 TURN RF CHOKE
565 TWO CHANNEL SCOPE
DIFFERENTIAL VOLT METER
SHEILDED PAIR
1.4 MM OD GLASS MICRO ELECTRODE WITH 5 MICRON TIP
COMPUTER OF AVERAGE TRANSIENTS
THERMOCOUPLE IN 1.4 MM GLASS TUBE
PROCESSING AMPLIFIER
RESPIRATORY PUMP
ANALOG TAPE RECORDER
PROCESSING AMPLIFIER
HEATING PAD
STIMULATOR
PROCESSING AMPLIFIER
TIMER
10 TURN RF CHOKE
561 A FOUR CHANNEL SCOPE
RECTAL TEMPERATURE CONTROL UNIT
TIMER MARKS
PROCESSING AMPLIFIER
EKG
STRIP CHART
1 MIL DIA. HIGH RESISTANCE WIRES

Fig. 11. Block diagram of instrumentation used to quantity CNS effects of microwave radiation in the cat.

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[1] 1 mil = 0.001 inch

a glass pipette with a sealed tip at the homologous point in the opposite thalamus (assuming the brain was symmetrical) at the same depth as the recording electrode. The thermocouple was removed during the exposure times to prevent any fringing field effects. The electrical response in the thalamus was recorded continuously with microwaves alternatively on and off in 15-min intervals over a total period of 8 to 12 h. The dosimetry was based on the methods described in the previous section. The EEG response was observed to increase with microwave power density and temperature at much higher levels than that required to produce thalamic changes. The thalamus response characteristics were recorded on an analog tape recorder processed for improved signal-to-noise ratio, both on-line and off-line, by a computer of average transients, and plotted by means of an x—y recorder. The technique was also used to assess evoked responses in other portions of the brain due to audio clicks, light flashes, and incident microwave pulses.

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SOME RECENT DEVELOPMENTS IN THE CHARACTERIZATION AND MEASUREMENT OF HAZARDOUS ELECTROMAGNETIC FIELDS

R. R. Bowman

Electromagnetics Division, National Bureau of Standards, Boulder, Colorado, U. S. A.

1. INTRODUCTION

Though some of this paper is relevant to the quantification of fields and energy deposition inside subjects, the discussion will be limited to the measurement of either fields external to subjects or fields unperturbed by subjects.

People and other subjects are often exposed to fields near radiators and in situations where a high level of multipath interference exists. The accurate measurement of such fields has been notoriously difficult. The purpose of this paper is to review briefly some developments over roughly the last five years that have provided some capability for making easy measurements of very complicated fields.

Since this paper is concerned with complicated fields, it is emphasized that the term "electric field strength" is used in the general sense and is defined as the Hermitian magnitude $|E|$ of the field. That is (using rectangular coordinates)

$$|E| \equiv (|E_X|^2 + |E_Y|^2 + |E_Z|^2)^{\frac{1}{2}} \qquad [1]$$

Similarly, magnetic field strength $|H|$ is defined by

$$|H| \equiv (|H_X|^2 + |H_Y|^2 + |H_Z|^2)^{\frac{1}{2}} \qquad [2]$$

Unlike the magnitude $|S|$ of the power density, which is often not a meaningful measure of the intensity of complicated fields, the Hermitian magnitudes are meaningful measures of the strengths of fields having reactive near-field components, multipath components, and arbitrary polarization (9).[1]

2. CHARACTERIZING HAZARDOUS FIELDS

For many years $|S|$ has been used as an index of potential hazards for microwave frequencies (frequencies above 300 MHz). For frequencies below 300 MHz, $|E|$ and $|H|$ are often used (6, pg. 78; 7, pg. 66) rather than $|S|$ mainly because at these lower frequencies: (a) subjects are often exposed to strong reactive near-field components for which $|S|$ is identically zero; (b) it can be important, particularly below 30 MHz, to know both $|E|$ and $|H|$; and (c) available instrumentation uses antennas that measure $|E|$ and $|H|$ separately. (Despite the need to know $|H|$ at some frequencies, the remainder of the paper will be limited to measurements of $|E|$).

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[1] Though $|E|$ is a proper measure of the strength of resonance fields, intense fields with high "O" may not be hazardous However, reactive near-fields should not be assumed to necessarily have high "O" values.

Despite the widespread use of $|S|$ above 300 MHz, it has often been noted that $|S|$ is a poor index of potential hazards even in the microwave band (9); and there is an increasing interest in using $|E|$ or some derived quantity such as $|E|^2$ or electric field energy density $U_E \equiv {}^1/_4\, \varepsilon_o\, |E|^2$. One reason for not using $|S|$ is that intense reactive near-fields can be important for frequencies at least as high as 1 GHz (for example, when subjects are close to or nearly touching leaking cracks). Also, intense standing-wave fields, at any frequency, can have little or no power density. Further, $|S|$ is quite difficult to measure unless one is fortunate enough to be concerned only with stationary, single-component, plane-wave fields with known polarization[2].

Undoubtedly, the recent increase in the use of $|E|$ at microwave frequencies is due to the development of instruments that can measure this quantity with extreme ease[3] over certain frequency ranges despite the presence of reactive near-field components, multipath components, and arbitrary polarization. While there are a number of possibilities for achieving such instrumentation, the author knows of only three types of instruments that have been developed to the degree that they are either advanced prototypes or production models. The latest of these three instrument types are briefly described in the next section[4].

3. RECENTLY DEVELOPED INSTRUMENTS MEASURING |E| IN COMPLICATED FIELDS

3.1. An Instrument Based on a Golay Cell

A broadband, isotropic field sensor was described by Fletcher and Woods (4) in 1969. The sensor is comprised of a pair of thin-walled air-filled spheres connected by tubes to a sensitive differential pressure transducer (see Fig. 1). One sphere is coated with a resistive film that is heated by the EM field to produce a pressure differential between the spheres[5]. The non-coated sphere provides compensation for changes in ambient temperature or pressure. This sensor is essentially a type of Golay cell (5).

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[2] At sufficiently high frequencies microwave propagation and absorption approximate those of light energy. For these frequencies reactive near-fields are not important with respect to hazards. Also, for multipath fields $|S|$ or $|E|$ measured separately for each component or, perhaps, averaged over the standing-wave variations would likely be better indications of the potential hazards than the maxima of the standing-wave variations. At the present time, the importance of reactive near-fields and standing-waves is not well enough understood to set a definite lower limit on those frequencies for which microwaves can be considered to behave like light waves as far as potential hazards are concerned. Failing definitive information, it seems reasonable that this lower limit should be between 5 GHz and 15 GHz.

[3] Within certain restraints explained later, the instruments are rigorously isotropic in that their response is independent of angular orientation about a given point in complicated fields; and they provide a direct measure of the field level (in various units) without requiring any special technique on the part of the operator.

[4] It is emphasized that the discussions in the following sections should not be interpreted as either endorsements or critiques of the instruments described. Except for the instruments described in Section 3.2, the author has not performed any evaluative measurements on these instruments. The information and data for the instruments described in Sections 3.1 and 3.2 are from the open literature. The reader is cautioned that not all of the important capabilities and limitations of these instruments are discussed in this brief paper. Interpretive comments by the author are believed to be either obvious or easily proven.

[5] Earlier, Schwan (8) had suggested the use of a spherical bulb filled with electrolyte for

Neglecting the perturbing effects of the other parts of the instrument, the symmetry of the energy-absorbing sphere insures that the response of the sensor will be independent of its angular orientation in fields of arbitrary complexity. Further, for wavelengths much longer than the diameter of the sphere and if the surface resistivity of the sphere is large enough, the response of the sensor will be determined to a good approximation solely by the value of $|E|^2$ at the position of the sensor regardless of the configuration of the field[6]. To the author's knowledge, the response of this type of sensor has not been established for arbitrary fields with wavelengths comparable with or shorter than the sphere diameter. (The issue is: what kind of average of $|E|^2$ will the sensor provide for standing-wave fields or reactive near-fields that have large electric field gradients over the sphere?) However, it has been shown that the sensor will have an essentially constant response for single plane-wave fields with wavelengths either long or short compared with the sphere (10).

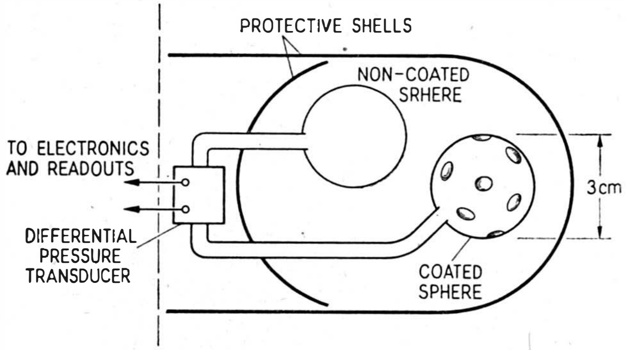

Fig. 1. Schematic representation of a wideband, isotropic field sensor. The field sensing sphere is coated with a high-resistivity film. The spots are regions of lower resistivity that provide an extended upper frequency response. The protective shells prevent temperature differences between the spheres due to either air currents or radiations above the microwave region.

An instrument using this type of sensor was marketed[7]. Some of its important characteristics are listed in Table 1. Some other important characteristics and limitations are discussed here. An important capability of the sensor is that it can be expected to accurately sum the intensities of multifrequency fields. A serious limitation is its slow response time of about 20 seconds (90 percent). Also, the sensitivity is rather limited, but perhaps further development could improve this limitation. The sensor can withstand fields of 1 watt/cm^2 average level (4), but the peak intensity overload is apparently not known.

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a field sensor, but apparently the slow rate of temperature rise of the electrolyte prevented a practical application of this type of sensor except for laboratory use.

[6] For long wavelengths the unperturbed electric field will be essentially uniform over the sphere for any field configuration. The currents in the coating when the sphere is introduced into the field will be due to the final tangential field over the sphere; and, for a large surface resistivity, the final tangential field will not differ significantly from the unperturbed field. Thus, the response of the sensor, to a good approximation, will not be affected by the magnetic field and the sensor will have the same response coefficient for $|E|^2$ in a reactive near-field or standing-wave field as it would for a simple plane-wave field.

[7] By the Wayne Kerr Company Limited, New Malden, Surrey, England. For reasons unknown to the author, it was subsequently removed from the market.

Table 1

Table of instrument characteristics

For instruments described in:		Section 3.1	Section 3.2	Section 3.3
Frequency range (GHz) for ± 1 dB response for single plane-waves		0.4 to 40	0.03 to 3[1]	0.85 to 15
Upper frequency (GHz) limit for spatial resolution of complicated fields.[2]		1.25	4.7	1.1
Field levels measurable[3]	Field strength $\|E\| \left(\frac{V}{cm}\right)$	0.34 to 3.4	0.009 to 47.5	0.09 to 6.1
	Equivalent plane-wave $\|S\| \left(\frac{mW}{cm^2}\right)$	0.3 to 30[4]	0.0002 to 6000[5]	0.02 to 100[6]

1. Can be extended to about 5 GHz by using a different detector-diode package.
2. These limits are somewhat arbitrarily chosen. They correspond to a wavelength for which the sensor dimensions are approximately 1/8 wavelength.
3. All three instruments respond essentially to $|E|^2$, but they are calibrated to read in different units. For purposes of comparison, their capabilities have been stated here in terms of $|E|$ and in terms of the power density in a simple plane-wave field with corresponding $|E|$.
4. Using only one probe.
5. Using three probes. Any single probe covers a dynamic range of 40 to 50 dB depending on the choice of input amplifier.
6. Using two probes. Each probe covers a dynamic range of 20 to 30 dB depending on the choice of input amplifier.

Note: some minor approximations have been made in order to simplify the comparisons in this table

3.2. An Instrument Based on Three Orthogonal Dipoles

A second type of broad-band, isotropic field sensor was described by Bowman, Larson, and Belsher in 1970 (2, 3). This type of sensor consists of three orthogonal dipoles with diode detectors connected between the arms of the dipoles. Each diode is separately connected to signal processing circuitry by a pair of high-resistance leads (see Fig. 4). The high resistance leads cause little perturbation of the field being measured and also provide powerful filtering so that only the DC value of the rectified signal at the diode is conducted to the electronics. For low intensity fields, and assuming wavelengths long compared to the dipoles, the detected signals from the orthogonal elements of the field sensor are proportional to the square of the corresponding electric field components. After equalizing the responses of the three channels, the summing amplifier output is proportional to $|E|^2$. For higher intensity fields, the non-linear characteristics of the summing amplifier provide extended dynamic range. The readout of the instrument is calibrated to display $^{1}/_{4}\varepsilon_0|E|^2$. For wavelengths up to perhaps two or three times the length (8 mm) of the dipoles, the probe can be calibrated to measure single plane-wave fields (or to provide some sort of average reading for multipath fields). The response of the probe will, of course, be much greater in the resonance region for the dipole.

Since orthogonal dipoles with common centers do not mutually couple, early models of this type of sensor placed the dipoles so that they had a common center. How-

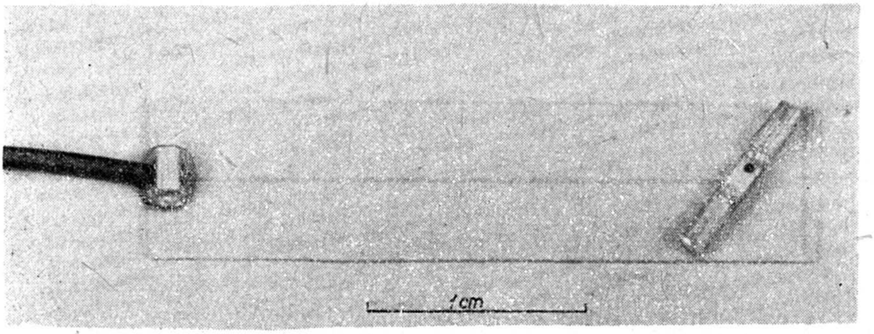

Fig. 2. Photograph of one of three identical elements that are fitted together to form a sensor with three orthogonal dipole-diode field detectors. The deposited thin-nichrome films on the substrate form a balanced twin-lead with linear resistances of about 50 kΩ/cm. The high-resistance twin-leads connected to the rear of the substrate are made of carbon-loaded Teflon and have a linear resistance of about 3 to 30 kΩ/cm (depending on the instrument model).

ever, this arrangement tends to maximize the "cross-talk" between the three pairs of high-resistance lines near the common center where significant, though small, differential-mode radiofrequency currents exist on these lines. Present models utilize the fact that the dipoles can be displaced from center without introducing a serious amount of coupling between the dipoles. Figure 2 shows one of three identical elements consisting of a dipole, diode, and deposited nichrome thin-film resistance lines, all located on a substrate. The acute angle between the dipole and the high-resistance leads is

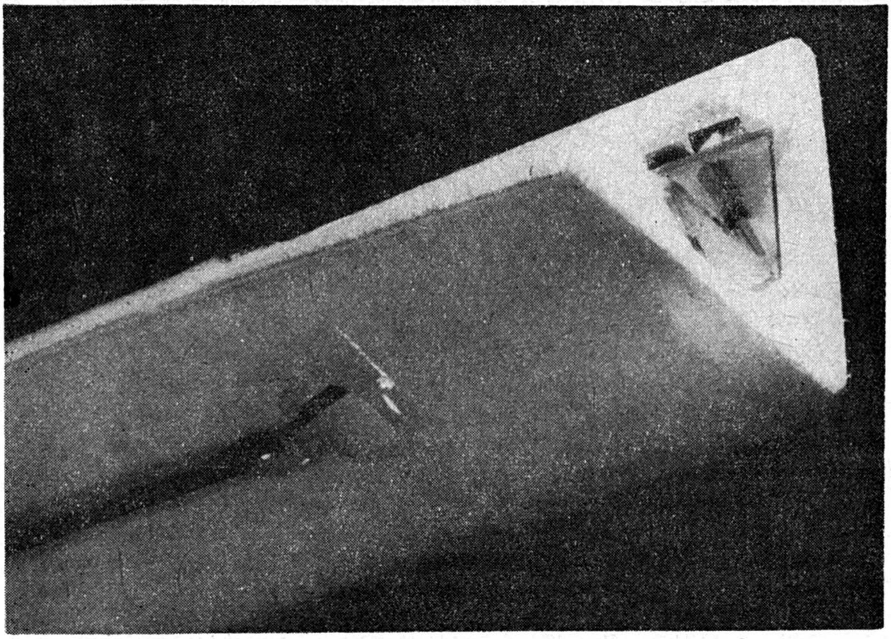

Fig. 3. Photograph of the field sensor assembled inside a low-density polyfoam support. The three identical elements (see Fig. 2) are fitted together to form a triangular cross section tube.

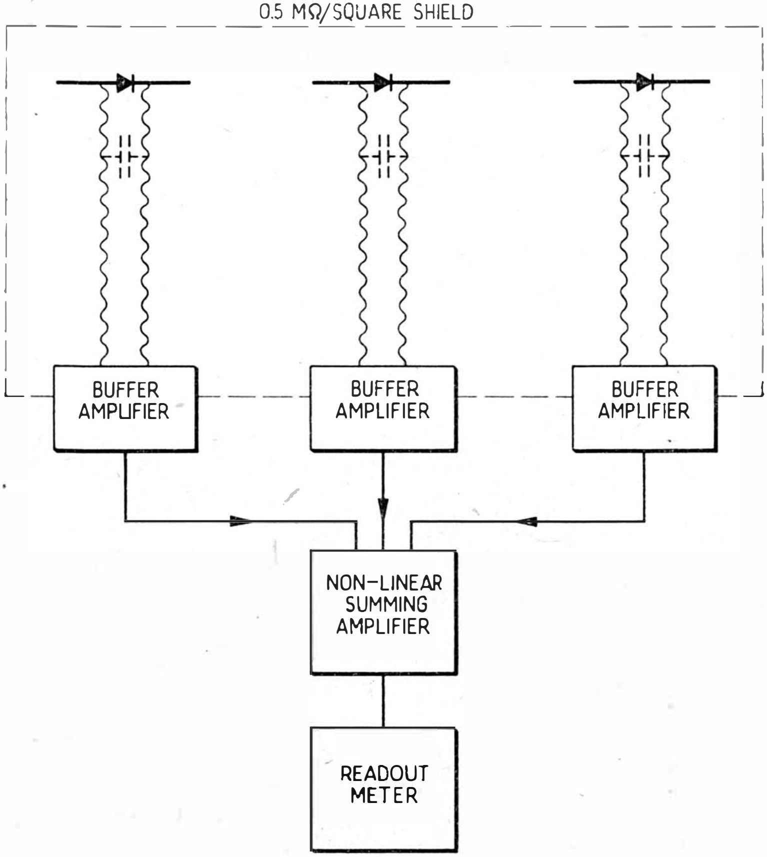

Fig. 4. Functional representation of the instrument described in Section 3.2. The dipole-diode field detectors are located at the end of a wand and the buffer amplifiers are located in the handle of the wand. (See also Fig. 5). The non-linear summing amplifier and readout electronics are connected to the wand by a cable (which can be 20 meters or more in length). Each probe channel can be read separately for test purposes and to determine the orthogonal components of the (electric) field.

54.74 degrees. This angle provides orthogonality between the dipoles when the three elements are placed together along the long edges to form a tube with an equilateral triangle for a cross-section. Figure 3 shows this tube inserted into a hole drilled in the end of a polyfoam support. The high-resistance lines connecting the elements to the electronics are made from carbon-loaded Teflon and can be almost any length desired. The polyfoam support is fitted snugly inside a thin-walled plastic tube (see Fig. 5) for protection. To reduce "capacitive" current noises in the high-resistance lines, the protective tube is coated with a slightly conductive layer which is bonded to the metal handle of the probe with silver-conductive glue.

As shown in Table 1, an important characteristic of this instrument is its sensitivity. It is the only instrument described here that is sensitive enough to measure the low intensity fields of interest to some countries. However, it must be emphasized that the present designs will provide accurate readings only for fields that do not have mo-

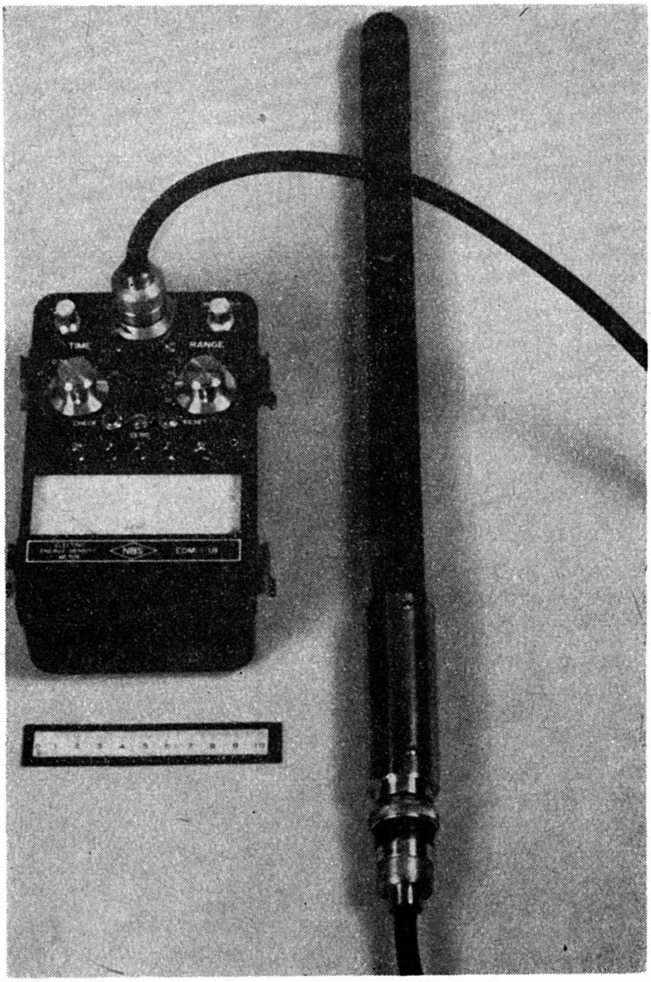

Fig. 5. Photograph of the instrument described in Section 3.2. The probe shown here is short (about 0.5 meters). For measuring fields at the lower end of the microwave band or below, the field sensor can be located in a wand 3 meters or more in length. The handle of the probe is metal and a high-resistance shield extends on the outside of the wand, providing a continuous shield for the probe to prevent "quasistatic" noise.

dulations that exceed the bandpass (approximately 0 to 3000 Hz) of the probes[8]. Another limitation of the instrument is that it will not accurately measure multifrequency fields. In multifrequency fields the instrument tends to read "high", but the error will not be greater than 3 dB if only two intense fields are present. Typically, the probes will withstand continuous wavefield intensities at least 10 dB greater than the highest measurable level. The peak intensity overload is not presently known.

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[8] Probes are under development that will read peak field levels for fields with repetitive wave forms, even fields with sub-microsecond rise-times.

3.3. An Instrument Based on Lossy Elements Made from Thin-Film Thermocouples

A publication by Aslan in 1972 (1) described another isotropic, wide-band field sensor. This field sensor is composed of three orthogonal lossy elements (see Fig. 7) that are heated by the field. Each element consists of a series of thin-film thermocouples (see Fig. 6) deposited on a plastic substrate. Assuming that the wavelength is long compared with the length (about 3 to 4 cm) of the thermocouple strips, and since the linear resistance of the strips is high enough to cause only slight field perturbations, the heating in each strip is directly proportional to the square of the original electric field component along it. The thermocouples provide a signal proportional to the heating, and the three outputs from the elements are conducted along high-resistance leads and then summed to provide a signal proportional to $|E|^2$. However, the instrument (see Fig. 8) is calibrated to read in units of mW/cm^2.

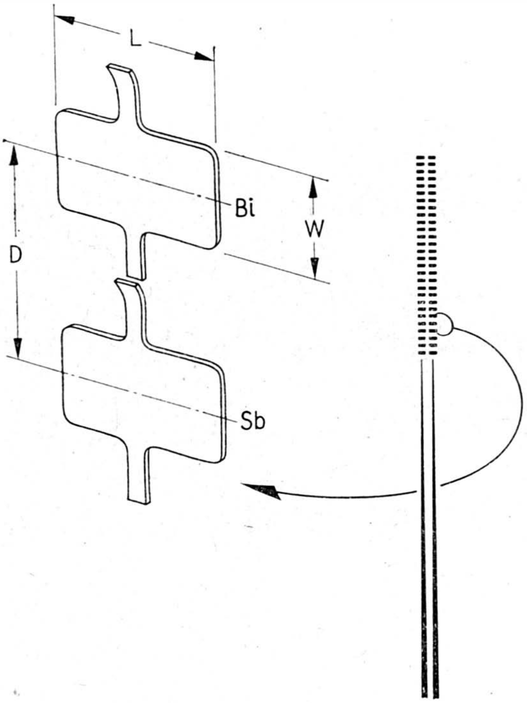

Fig. 6. Field sensor element with distributed thin-film resistive thermocouples (Antimony-Bismuth). Tapered resistive-film leads reduce interaction between leads and elements. Owing to the higher resistance of the narrow portions of the elements, most of the heating occurs there. The broad portions of the elements provide a heat sink to the ambient air. Three elements are orthogonally arranged as shown in Fig. 7.

Referring again to Figure 6, nearly all of the heating occurs in the narrow portions of the thermocouples. The wide portions provide "heat sinks" to the substrate and to the ambient air. This arrangement provides a low ambient-temperature sensitivity (less than 0.05 percent C).

For single plane-wave fields the type of sensor described above has an essentially constant response coefficient for a wide range of wavelengths both larger and smaller than

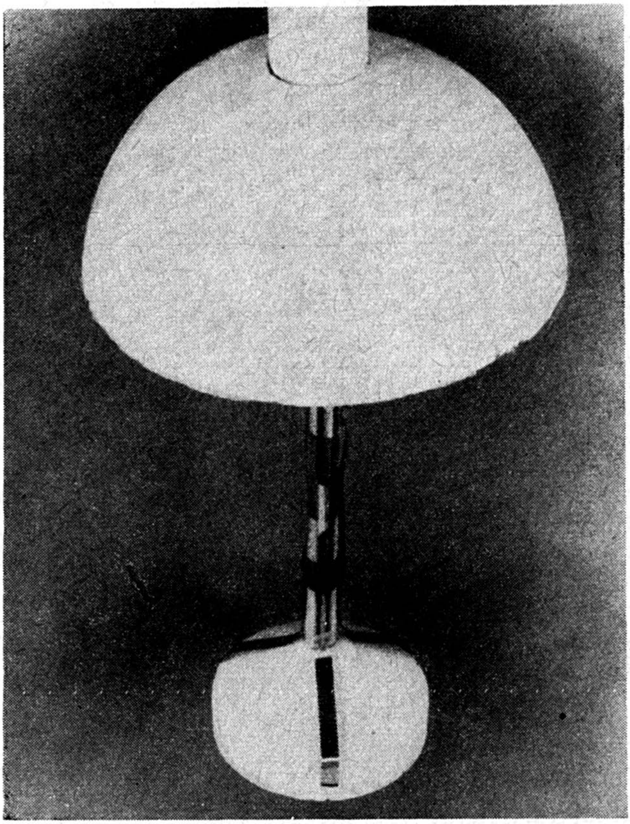

Fig. 7. Internal view of the probe. Three field sensing elements (see Fig. 6) are arranged orthogonally on a low-density polyfoam support. The support is located inside a 10 cm diameter low-density polyfoam sphere.

the lengths of the elements. For complicated fields one would expect that the sensor would provide some sort of average of $|E|^2$ over, roughly, the volume of a sphere circumscribing the sensor. However, it has not been shown, to the author's knowledge, that this average would be the simple average of $|E|^2$. In fact, it is easy to show that the sensor can give a zero reading when the average of $|E|^2$ is not zero[9]. This limitation may not be very serious since a reasonable indication of the average strength of the field can probably be obtained as the probe is moved throughout the field region of interest.

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[9] Imagine a standing-wave field composed of two travelling waves of equal magnitude and opposite directions. Assume a wavelength smaller than the length of the elements of the sensor so that the multipath field will have strong gradients within the volume of the sensor. If the sensor is oriented so that the apex of the orthogonal elements is at a point of zero field strength and one of the elements is parallel to the electric field direction, the output of that element will be zero. Since the other two elements will be orthogonal to the electric field their outputs will also be zero. Thus, the instrument reading will be zero even though the average of $|E|^2$ could be very large over the volume of the sensor. Further, the response of the sensor will not be independent of its angular orientation at the field point.

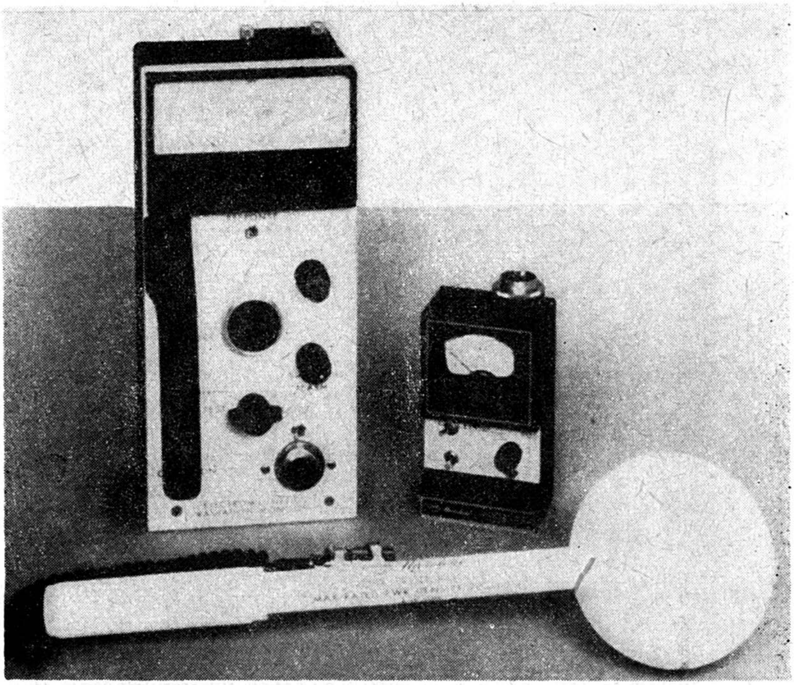

Fig. 8. Photograph of the instrument described in Section 3.3. The larger electronics unit provides additional features such as recorder output and audible alarm.

As shown in Table 1 this instrument has fairly good sensitivity[10]. It has rather limited capability to resolve intensity variations in the field, but perhaps this limitation can be reduced with further development. The instrument can accurately measure multi-frequency fields. The overload for continuous wave fields is 100 to 300 mW/cm^2 and the peak overload is 20 to 60 watts/cm^2, depending on the probe model.

4. CONCLUDING REMARKS

The need to measure easily very complicated fields for the evaluation and control of hazardous emissions has resulted in several instruments that have considerable capability for this difficult measurement task. Though they all have serious limitations, these, and other, instruments are still evolving rapidly. It is reasonable to believe that instrumentation will soon be available to permit easy measurements for nearly all hazardous emissions of interest.

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[10] An instrument of this type has been marketed by the Narda Microwave Corporation, Plainview, New York, U. S. A.

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METHODS OF CALIBRATING MICROWAVE HAZARD METERS

R. C. Baird

Electromagnetics Division, National Bureau of Standards, Boulder, Colorado, U. S. A.

INTRODUCTION

Accurate and reliable measurements of microwave radiation are required for hazard surveys, leakage detection, testing of products for compliance with regulations, and for determining exposure levels in experiments designed to investigate the biologic effects of microwave radiation. Accurate calibration of the instruments used for these measurements is essential for safety reasons and to provide a basis for comparison of the experimental results of various laboratories.

Existing calibration methods require that a known field intensity be established through measurement, calculation, or a combination of both. The device under test is placed in the "standard" field and the meter indication is compared with the known field value. This paper describes three different approaches to the problem of producing the "standard" calibrating field: 1) the free-space standard field method, 2) guided wave methods, and 3) the standard probe method. The first method is discussed in somewhat more detail than the other two because it is presently more widely used. Due to space limitations, all discussions are limited to descriptions of the basic concepts, the advantages and limitations, and estimates of the accuracies attainable with each method. An effort was made to include references adequate to enable interested persons to fill in the details. This was not always possible because some recent work has not been published and there are some problems that need further investigation.

FREE-SPACE STANDARD FIELD METHOD

There are several variations of this method, but the objective is always to establish a known calibrating field in free space. The most common experimental arrangement is shown in Figure 1. The power density $|S|$ at a point on the transmitting axis at a distance d from the transmitting antenna is given by

$$|S| = \frac{P_T G}{4\pi d^2} \qquad [1]$$

where P_T is the net power delivered to the transmitting antenna, and G is the effective gain of the transmitting antenna. The gain is normally determined in advance, and P_T and d are measured as part of the regular calibration procedure.

The most convenient method of determining P_T is by means of a dual directional coupler as indicated in Figure 1. The incident power P_i and the reflected power P_r are monitored with the coupler sidearms, and P_T is obtained from the relation $P_T = P_i - P_r$. High quality, broad-band couplers are available, along with methods for

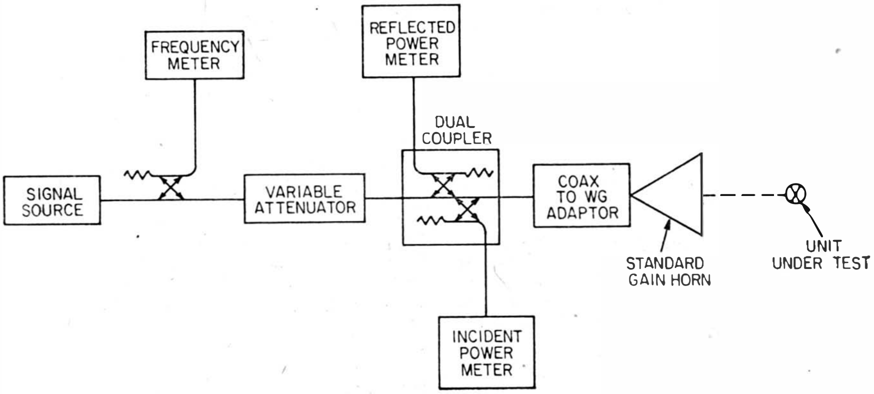

Fig. 1. Diagram of the basic experimental arrangement required for the free-space standard field method.

using them to determine P_T (4, 8, 9, 10). The methods cited are for calibrating power meters but the same techniques can be applied to antennas. The coupler described in (10) can be used from 0.3 to 8.5 GHz to determine P_T to within 1 or 2 percent* if corrections are made for mismatch effects. The foregoing assumes that the device being calibrated is sufficiently small and far enough away that the amount of energy reflected back into the transmitting system is insignificant. If this condition cannot be met, it is possible to obtain a correction for the effect of the reflected energy by varying d, observing the (approximately) sinusoidal variations in P_r, and then averaging P_r over at least one full cycle.

The principal sources of error in this method are uncertainties in the gain determination and multipath interference. Multipath effects are often overlooked, but every calibrating facility will have some scattering associated with it which may cause the field in the calibrating region to be significantly different from that predicted by equation 1. Even high-quality anechoic chambers are not perfect and, in fact, they are often worse than the user is led to believe. It is difficult to adequately evaluate this error and a treatment of the subject is beyond the scope of this paper. A useful discussion of the problem is given by Bowman (2).

When the multipath and gain problems are combined, one is indeed faced with a dilemma. The most accurate gain values are obtained for large distances, but large distances require greater transmitter power and the multipath situation is worse. On the other hand, there are some fundamental difficulties associated with accurate gain determinations at short distances. It will be instructive to take a closer look at these problems, particularly as they relate to so-called "standard gain horns". These pyramidal horns are commonly employed as radiators because they are rugged, stable, cover a relatively broad frequency band, and the problem of determining their gain has received a lot of attention.

The effective gain G of any antenna is a function of distance and approaches a constant G_0 as d approaches infinity. This is illustrated in Figure 2 which shows the estimated gain reduction for a representative example (13) plotted as a function of the parameter $n = d\lambda/a^2$, where a is the largest aperture dimension and λ is the free space

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* The uncertainties stated here are intended to include all known, significant sources of error and correspond roughly to 95 percent confidence limits. However, uncertainties quoted from the published literature should be interpreted as indicated in the original article.

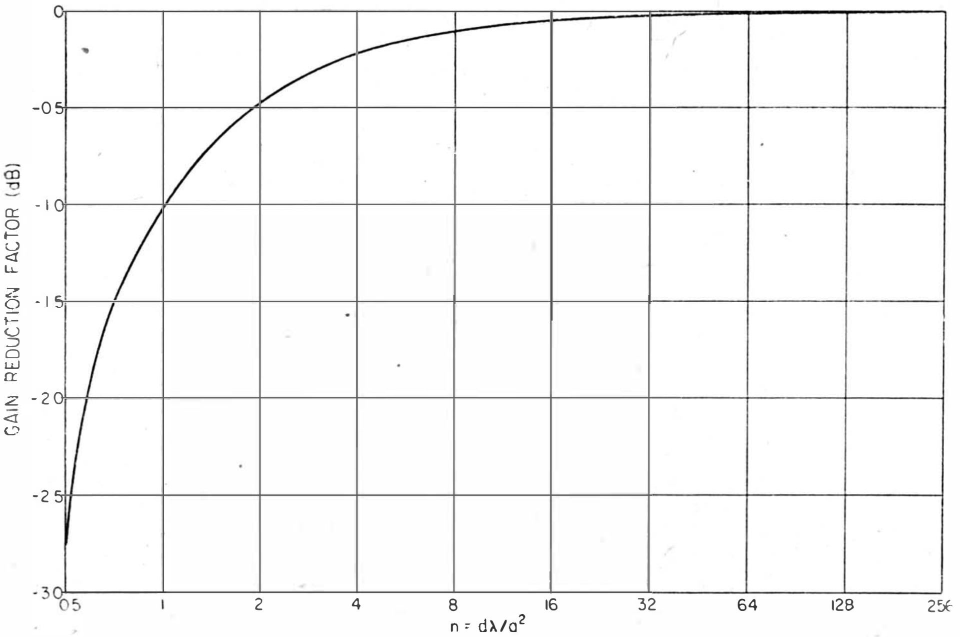


Fig. 2. Estimated near-field gain reduction for a pyramidal horn based on the method of Jull (13).

wavelength. In establishing a calibrating field, one must use the correct value of G for the specific distance involved; otherwise significant errors can result. The far-field gain G_o can be calculated to sufficient accuracy ($\simeq$ 0.3 dB) for many purposes (5, 11, 13, 16, 18) and may be measured to within about 0.1 dB if necessary (2, 6, 12, 14, 15, 19, 20). The values of G_o obtained by these methods hold for $d \gg a^2/\lambda$ (i.e., large n values). For distances greater than about one or two a^2/λ, it may also be possible to calculate G to within about 0.3 dB for pyramidal horns (13). However, the accuracy of these near-zone calculations has not been definitely established.

There are also problems in experimentally determining the near-field gain. The usual gain measurement approach involves measuring the power transmitted between a pair of antennas and applying the equation

$$G_T G_R = \frac{P_R}{P_T}\left(\frac{4\pi d}{\lambda}\right)^2 \qquad [2]$$

where P_R is the received power, G_T and G_R are the gains of the transmitting and receiving antennas, respectively, and d is the distance between the antennas. Equation [2] holds rigorously only in the far field. At shorter distances, G_T and G_R cannot be separated into the individual factors (19). Since one can always measure P_R/P_T, it is tempting to apply equation [2] to the case of two identical antennas in the near-field and obtain $G_a^2 = (P_R/P_T)\,(4\pi d/\lambda)^2$, where G_a is the measured apparent near-field gain of the two antennas. However, G_a obtained in this manner is not the correct near-field gain. In other words, G_a will not give the correct on-axis power density when used in equation [1]. This can perhaps be seen intuitively. P_R is the result of an integration (or averaging) of the incident field distribution over the receiving aperture, and unless the incident field is a plane wave, there is no simple relationship between G_a

and the desired on-axis power density. The error will, of course, increase as d becomes smaller.

This problem can be partially overcome in at least two ways.

1. If one antenna is small (an open-ended waveguide for example) and its far-field gain is known, it can be used to measure the on-axis gain of a larger antenna at relatively short distances. The measurements should be reasonably accurate ($\simeq$ 0.5 dB) so long as d is greater than about eight a^2/λ for the small antenna and more than one or two a^2/λ for the large antenna. The dimensions of the probe being calibrated should also be less than the aperture dimensions of the small antenna. This procedure was followed by Woods (21) who claims an overall uncertainty in the calibrating field of ± 0.5 dB from 1 GHz to 18 GHz and ± 1 dB up to 35 GHz.

2. When it is necessary to calibrate large numbers of nominally identical hazard meters, the extrapolation method described in (15) is particularly useful when applied as follows. Let B_d be the meter indication with the probe at an arbitrary near-field distance d, and B_o the indication with the probe at a large distance d_o where far-field conditions hold. We can write the relations where $|S|_o$ is the far-field power density, $|S|_d$ is the equivalent plane-wave power density in the near-field, and K is

$$B_o = K|S|_o, \quad B_d = K|S|_d, \tag{3}$$

a proportionality factor which relates the meter indication to the incident power density. In the extrapolation technique, B_d is measured over a range of distances and a power series is fitted to the product $B_d d^2$ over the measurement interval. This series is then used to determine $B_o d_o^2$ by extrapolation. One can then obtain the ratio

$$\frac{B_d d^2}{B_o d_o^2} = F_d \tag{4}$$

Substituting for B_d and B_o from equation [3], we obtain

$$|S|_d = F_d S_o \left(\frac{d_o}{d}\right)^2 = \frac{F_d P_T R_T}{4\pi d^2} \tag{5}$$

since $|S|_o = P_T G_T/(4\pi d_o^2)$. P_T can be measured, and G_T (the far-field gain of the transmitting antenna) can be obtained by the extrapolation method or other methods previously referred to. The near-field correction factor F_d is a function of d, and must be determined for every combination of radiator and type of probe. However, once F_d has been obtained for a given probe, it can be used to calibrate other probes of the same type with little additional error.

It should be pointed out that, for rectangular apertures

$$|S| \simeq \frac{\varepsilon P_T}{n^2 A_p}\left(\frac{b}{a}\right)^2 \tag{6}$$

where ε is the aperture efficiency, $A_p = ab$ is the physical area of the aperture, and a and b are the aperture dimensions (a being the largest). For horns of a given design, the ratio b/a and ε are approximately constant, so the power density for a particular value of n is inversely proportional to the aperture area. It is desirable to have n as large as possible to reduce the gain uncertainty; therefore, if P_T is limited, it is necessary to use smaller apertures in order to achieve the required calibrating field intensity.

At the National Bureau of Standards we presently use standard horns above 2.6 GHz to establish 10 mW/cm² fields to an accuracy of ± 0.5 dB, including multipath effects. The required transmitter power is only 10 to 20 watts. Below 2.6 GHz we use an open-ended waveguide as the radiating element. The gain calculations for horns do not give accurate results for the waveguide, so the gains are measured by the techniques described in (15). Present accuracy down to 0.9 GHz is ± 0.6 dB. Transmitter powers of 35 watts or less are required to produce a 10 mW/cm² field. We believe open-ended guides can be used down to about 0.3 GHz and are in the process of determining the accuracy of this method over the 0.3 to 0.9 GHz range.

GUIDED WAVE METHODS

The fields inside a waveguide can be accurately calculated and, in some cases, are sufficiently uniform to be considered for calibration purposes. The main advantage of such a system is that considerably less power and space are required. One disadvantage is that the maximum transverse dimensions of the structure must be less than $\lambda/2$ for the highest calibration frequency in order to avoid higher order modes which result in complicated field distributions. Hence, the method is only useful for frequencies below 1 or 2 GHz, since the device being calibrated must be small compared to the guide dimensions.

Figure 3 shows how a section of a rectangular waveguide can be used for calibrations. A reflectionless load is connected to the output end to prevent standing waves which would cause serious errors in the calibration. The probe to be calibrated is inserted into the waveguide through a hole in either the top or side wall and positioned in the center of the guide where the field is most nearly uniform. The access holes should be as small as possible. Equations for calculating the field distribution from P_n (the net power delivered to the section) and the guide dimensions can be found in any book on waveguide theory. P_n is determined in the same way as P_T in equation [1].

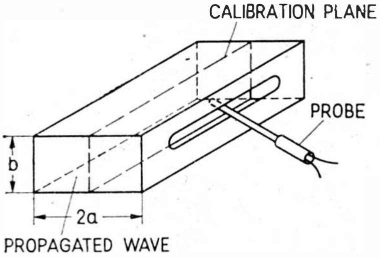


Fig. 3. A section of rectangular waveguide modified for use as part of a probe calibration system.

It is difficult to estimate the total uncertainty of this method because the field intensity will be modified by the size and nature of the probe being calibrated. Woods (21) describes a system which operates from 400 to 600 MHz with an estimated uncertainty in the field intensity of ± 12 percent. Aslan (1) uses a waveguide set-up at 2450 MHz which he believes is accurate to within ± 6 or 7 percent, based on comparisons with free-space measurements using a standard gain horn.

An example of a different type of guided wave structure which has been used at the National Bureau of Standards is illustrated in Figure 4. The basic unit is a section of two-conductor transmission line operating in the transverse electromagnetic mode (TEM), hence we call it a TEM Transmission Cell. As shown in the Figure, the main body of the cell consists of a rectangular outer conductor and a flat center conductor located midway between the top and bottom walls. The dimensions of the main section and the tapered ends of the cell are chosen to provide a 50-ohm impedance along the entire length of the cell — see (7, 17) for some design information. When the cell is carefully made and terminated in a reflectionless load, the input VSWR is usually less than 1.05 and always less than 1.1 for all frequencies below the cut-off limit. The field

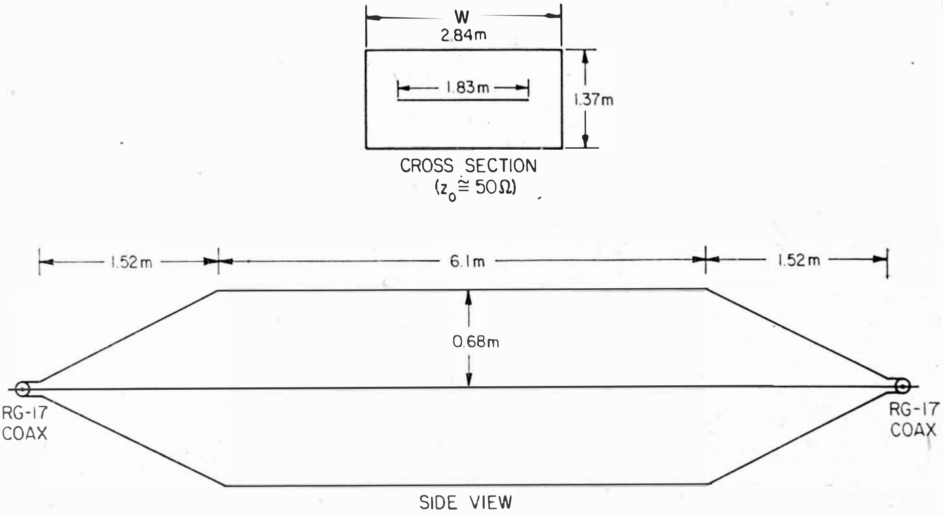


Fig. 4. A type of TEM Transmission Cell used at the NBS for calibrating hazard meters and for measuring susceptibility of electronic equipment to EM fields. These cells can also be used as exposure chambers for studying biologic effects.

intensity in the center of the cell can be quite uniform as shown in Figures 5 and 6, and the wave impedance throughout the cell is very close to the free-space wave impedance as shown in Figure 7. These features are the principal reasons for using this type of cell for calibrations.

The E-field in the center of the cell, half way between the center conductor and the top (or bottom) wall, will be vertically polarized and is given by

$$E_v = \frac{\sqrt{P_n R_c}}{d}, \qquad [7]$$

where R_c is the real part of the characteristic impedance of the cell, and d is the distance from the upper wall to the center plate. P_n (the net power delivered to the cell)

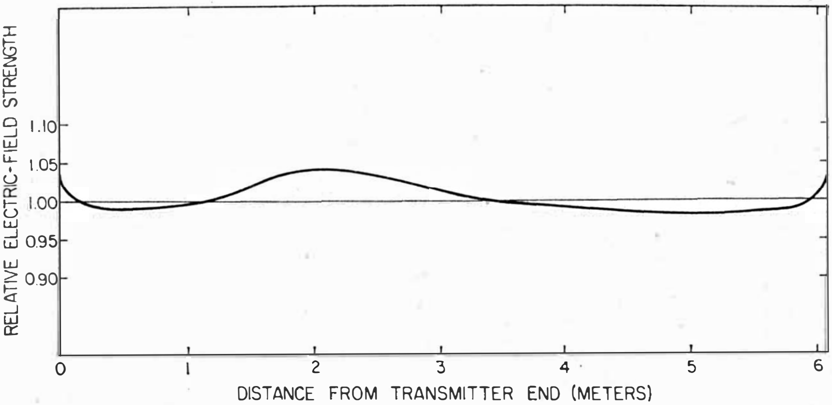


Fig. 5. Relative longitudinal E-field distribution of TEM Cell measured along the center line of the cell 30 centimeters above the center strip.

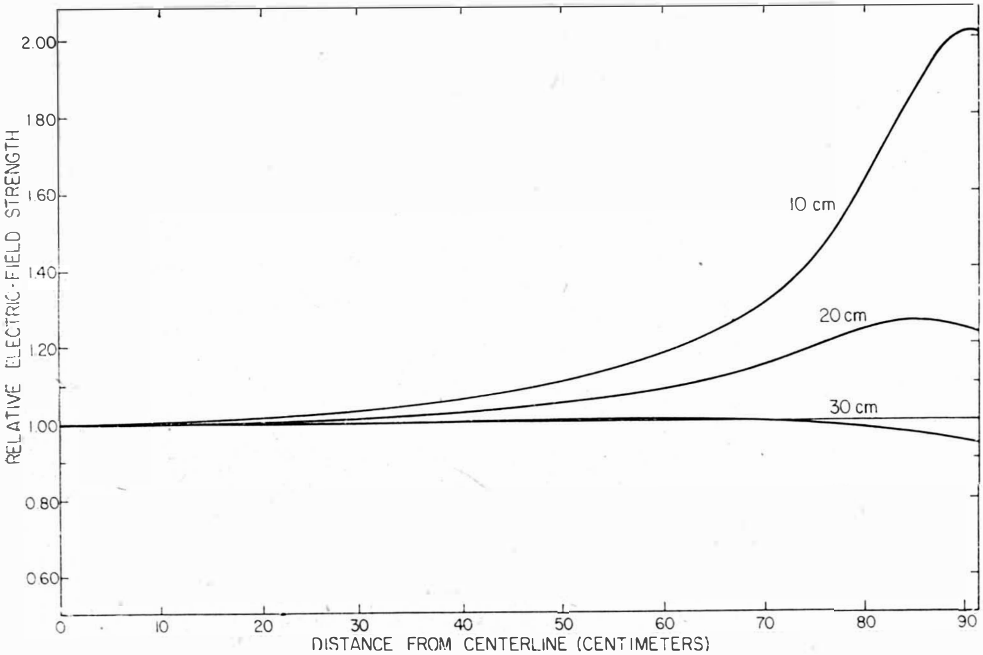
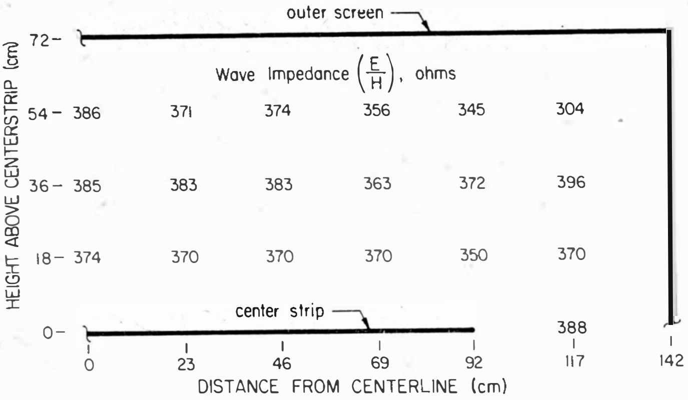


Fig. 6. Relative E-field distribution of TEM Cell measured in a transverse plane midway between the ends at three heights above the centerstrip.


outer screen
center strip
Wave Impedance $\left(\frac{E}{H}\right)$, ohms
72
142
HEIGHT ABOVE CENTERSTRIP (cm)
DISTANCE FROM CENTERLINE (cm)

HEIGHT ABOVE CENTERSTRIP (cm)	0	23	46	69	92	117
54	386	371	374	356	345	304
36	385	383	383	363	372	396
18	374	370	370	370	350	370
0						388

Fig. 7. Calculated values of wave impedance for the TEM Cell in a transverse plane midway between the two tapered ends.

is determined in the same way as P_T. We have used a time-domain reflectometer to determine R_c. The introduction of the probe into the test region will change R_c and alter the field distribution slightly, but if the probe is much smaller than the transverse cell dimensions, this error will be small. Although we have not fully evaluated the errors associated with this method, we believe the total uncertainty can be kept below ± 1 dB. We have used these cells to generate fields of 10 V/m to 500V/m from dc to 600 MHz, but a practical upper frequency limit for accurate calibrations may be somewhat lower ($\sim$500 MHz), depending on the size of the device to be calibrated. The cells can be made in various sizes to suit particular needs, but the width (W in Fig. 4) must be less than $\lambda/2$ at the highest design frequency.

STANDARD PROBE METHOD

This method is the simplest, and it may ultimately prove to be the best method of calibrating hazard meters for general use. The idea is to have a stable and reliable probe that has been accurately calibrated and use it as a "transfer standard". That is, the standard probe would be used to determine the field intensity over a particular region in space (or in a guided system) produced by an arbitrary transmitting antenna. The probe to be calibrated would then be placed in the same location in the field and the meter reading compared with the known value of the field. The only requirements on the transmitter are that it generate a field which has the desired magnitude, is constant in time, and is sufficiently uniform over the calibrating region.

A dipole-diode probe of the type developed by Bowman (3) can probably be improved to the point where it could serve as such a transfer standard. These probes have a nearly isotropic response pattern and a large dynamic range ($\gtrsim$ 40 dB); they are rugged, practically burn-out proof, can be made very small (1 or 2 cm in diameter), and it may be possible to cover the entire frequency range of 10 MHz to 3 GHz with a single probe. Further improvements in the temperature coefficient and in the response pattern of the probe are still needed, but are believed to be possible. The total uncertainty of this method would probably be less than about 0.5 dB. The biggest advantages of this approach are convenience, reliability, and simplicity.

CONCLUSION

Several methods of calibrating hazard meters have been discussed and the uncertainties associated with each method were estimated. It is important to understand that one cannot expect to achieve the same accuracy when using the meters for practical measurement applications. Some of the reasons are as follows.

1. Hazard meters are usually calibrated in nominally plane-wave fields. Such fields are seldom encountered in practice, and the sensor may not respond in the same way to non-planar fields.
2. In most calibration methods, only the sensor (probe) is exposed to the field, while in practice the complete system, including the indicating unit and connecting cable, is immersed in the field.
3. With hand-held meters, the presence of the operator can significantly affect the reading.

The additional uncertainty caused by these factors is difficult to assess and will vary with the type of meter. However, if good measurement procedures are followed, accuracies of ± 1 or 2 dB can probably be achieved in practice.

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METHODS OF MICROWAVE FIELD QUANTIFICATION FOR BIOLOGIC STUDIES

R. B. Smith

Postgraduate School of Electrical and Electronic Engineering, University of Bradford,
Bradford, United Kingdom.

In the United Kingdom, as in many countries, a continuous increase in the use of high-power microwave sources for radar, communication and heating applications, as well as the rapidly expanding literature on microwave radiation hazards, is resulting in a re-examination of the permissible radiation and emission levels and the means by which these levels are monitored. At the present time, there exists a United Kingdom national recommendation, which has been endorsed by the United Kingdom Medical Research Council, of a radiation level of 10 mW/cm^2 as a maximum limit for the continuous exposure of personnel. These levels are not intendend to be applied to therapeutic exposure under medical supervision.

Recently, in response to a number of requirements from sectors of United Kingdom industry and other official bodies, the Telecommunication Standards Committee of the British Standards Institute set up a technical committee to produce recommendations and prepare a British Standard on the "Safety of Telecommunication and Electronic Equipments, Components and Devices". This committee (TLE 23) consists of representatives from all the major United Kindgom telecommunication and electronic manufacturing industries, the Post Office, the Broadcasting Authorities, Government, Departments, National Research Organizations, technical branches of the Services, the Gas and Electricity Authorities, the Universities, oil companies and other organizations, together with such advisory bodies as the Medical Research Council, the United Kingdom Atomic Energy Authorities and various Government Department Safety Services.

The Committee is in the process of drafting a British Standard Guide, various parts of which are primarily intended for use by those concerned with the design, manufacture and usage of telecommunication and electronic equipment and the specifications and conditions of use of this equipment. It is intended that this guide will provide basic and fundamental information concerned with the hazards which may arise due to the design, operation and environmental conditions experienced with all types of telecommunication and electronic equipment. Standardized reproducible tests designed to assess the degree of safety in particular circumstances will be described, and recommended preferred methods of avoidance of possible hazards will be stated.

The Guide will be produced in a number of parts. The first part is intended to describe such general aspects as definitions and will include a method of classifying the seriousness of possible hazards of particular conditions of use for reference by manufacturers or users. All aspects, such as the stresses to which equipment might be subjected and the environmental conditions of use, the ability and training of personnel likely to have access to the equipment and the degree of such access, will be stated.

Subsequent parts of the Guide will describe the various hazards, their effects and suggested methods of protection, together with other related matters; attention will also be drawn where this is necessary to the anomalies and inconsistencies which may at present exist in other documents and indicate the preferred values and safety levels.

Subjects proposed for subsequent parts of the Guide are:

- — Hazards associated with the use of electrical power in electronic equipment.
- — Hazards associated with high and low temperatures.
- — Mechanical, chemical and fire hazards associated with the use of electronic equipment.
- — Radiation hazards.

Radiation hazards embrace:

- — Ionizing radiation (X-rays, radioactive valves and substances and high voltages etc.).
- — Hazards from light sources (ultraviolet light, infrared and lasers).
- — Radio-frequency induced ignition and detonation.
- — Non-ionizing radiation (the effects of non-ionizing radiation between 300 kHz and 30 GHz).

Priority has been given to the preparation and drafting of the part concerned with radiation. Working Parties have been established within the Committee to prepare draft recommendations on these sections. The Working Parties concerned with these activities are composed of experts and specialists in the particular field and are recruited from research organisations, universities, industry, and various Government Departments. A Draft for Development is being prepared by the Working Party responsible for the section on non-ionizing radiation hazards. The purpose of this Draft is to review the effects of electromagnetic radiation on the human body and to describe the work that has already been carried out, to determine the now acceptable power density which is considered safe for personnel engaged in, or working in the vicinity of, high-power radio frequency sources.

Radiation and emission standards and methods of monitoring power density are certainly important factors in maintaining a safe working environment. However the equipment manufacturer and the user are not expected to accept responsibility in setting radiation standards although they may possibly be expected to assume some degree of responsibility in monitoring power density and in ensuring that the standards are upheld.

In the United Kingdom the range of instruments produced by Narda are extensively used to measure power density. However, a programme of research on a novel type of radiation monitor was conducted in the United Kingdom by Fletcher and Woods (1) at the University of Surrey. Although this work did not result in a commercial instrument, it may be worthy of further consideration. The basic aim of the work was to produce an instrument which would measure the sum of the power densities due to any number of sources over a very wide frequency range. Measurement was to be independent of the direction of the incident power and of the angle of polarization. To this extent it would be similar to absorption by the human body.

The instrument is a bolometer based on the classical gas thermometer. Two thin-walled silica spheres are placed close together in a protective radome. The radome is coated to reflect infrared radiation, is transparent to microwave radiation and protects the spheres from unwanted draughts. The spheres are air-filled and connected by narrow diameter tube to a capacitive differential-pressure transducer. One sphere is coated with a resistive film and absorbs microwave energy. The other sphere is not coated and provides ambient temperature compensation. The pressure difference due to the absorption of energy by the resistive film and subsequent heating of the air in the coated cylinder is converted into a change in capacitance at the pressure transducer. A special transformer ratio bridge converts the capacitance change into an out-of-balance voltage which is linearly related to temperature rise in the coated sphere and thus to the power absorbed.

The final temperature of the coated sphere is dependent on the heat loss mechanisms within the radome. The thermal time constant was found to be dependent mainly on the silica substrate and was about 8s for 63% of the final temperature. The use of an electronic differentiation circuit reduced the effective time constant of the instrument to less than one second.

A major part of the work was devoted to measuring the frequency-dependence absorption coefficient of the coated spheres. Absorption coefficient is defined as the ratio of the power absorbed by the sphere to the power incident on the area of cross-section of the sphere. Absorption coefficient was found to be a function of sphere diameter and surface resistivity. For the 3 cm diameter spheres chosen, the frequency response showed a damped resonance effect for coating resistivities below 5 kΩ/sq. The centre frequency occurred when the wavelength was approximately equal to one quarter of the sphere diameter. The maximum absorption coefficient of 1.77 was for a coating resistivity of 200 Ω/sq, about half the wave impedance. These results were confirmed theoretically by Williams (2). A coating resistivity of 5 kΩ/sq gave a reasonably uniform response from 400 kHz to 5.5 GHz. Additional spots or platelets of surface resistivity 200 Ω/sq painted on the surface of the resistive film extend the frequency response to 35 GHz.

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RADIATION HAZARDS FROM MICROWAVE SOURCES WITH MOBILE ANTENNAS: CERTAIN TECHNICAL PROBLEMS

Z. Frank

Institute of Aviation Medicine, Prague, Czechoslovakia

The problems of the interaction between microwave radiation and man may be considered from many points of view; detailed references may be found in recent publications by Gordon (3) and Marha (4). It may by assumed that the possibility of deleterious health effects is sufficiently well documented. In considering hygienic problems legal safe exposure limits should be taken as a starting point. Particular attention in considering hygienic conditions in a given locality should be paid to microwave sources, the main function of which is to emit energy into the environment. Typical sources of this kind are radar installations.

The obiectivity of the evaluation of hygienic conditions depends on certain basic conditions, i.e. the choice of the measured physical parameter of the radiation, the choice of the measuring equipment and methods, as well as the methods of evaluation of results. These basic conditions will be not discussed here and are taken for granted. Mumford's paper (5) may be considered as the best source of data concerning technical aspects of hygienic evaluation of microwave hazards. These aspects are inherently related to the theory of antennas and microwave propagation. In the present state of the art the general practice is to measure the intensity of the irradiated field, the basic conditions being a certain minimal distance between the sensor and the emitting antenna.

It should be pointed out that real conditions during field measurements of microwave intensity differ great from those of calibrating stands and in anechoic chambers To evaluate the permissibility of the conditions for human exposure it is necessary to determine the maximal intensity values. These change in time according to the regime of work of radar equipment, the changes being in most cases aperiodic. Moreover the radiation emitted from several independent sources simultaneously should be taken into account. The question arises of how to approach the problem of valid evaluation of the hygienic conditions in the case of sources with mobile antennas. The principal consideration is of course the health safety of the exposed individual. It should be, remembered, however, that overestimation of the hazards may have serious economic consequences. The aim of this paper is to present certain approaches to the problem of evaluation of the hygienic conditions.

Measurement of fields irradiated by various radar types are made using thermistor sensors and the measured parameter is the power density. If the measurements are made at various distances with the antenna immobile, varying the distance and position in respect to the axis of the beam, a certain spatial horizontal characteristic of the power density is obtained. If these results are analyzed and idealized (i.e. reflections are neglected) a characteristic power density distribution may be obtained for a given type of radar. This does not allow of course for movement of the antenna and the "intermittent" type of exposure, which is illogical. Such procedure is used, however, to define safe and hazardous zones.

This procedure is inconvenient because it is time consuming and needs complex calculations. It should also be stressed that the real hygienic conditions are different from such bidimensional characteristics and change with a change in the direction of the radiated beam. This procedure cannot be used in the case of a projected new localization for a radar installation. In such a case an approximate calculation may be made and the permissibility of such a proposed localization evaluated. Theoretically it is possible to predict the field intensity at an arbitrary point given the characteristics of the antenna, the power of the source and characteristics of the terrain along the direction of the beam. These theoretical predictions differ in many instances from the results of practical measurements in real conditions.

It may be difficult to determine the power density distribution in the case of certain directional antennas on the basis of diagrams of radiation characteristics. In theory there exist numerous formulas for the determination of antenna characteristics. In practice, however, it is necessary to verify theoretical calculations by practical measurements. Several of the variables important from the point of view of hygienic-technical considerations are unknown. The problem may be reduced to the question of adequate formulas for the determination of directional characteristics of the antennas on the basis of their design and dimensions. Such formulas are valuable for hygienic-technical services.

The problem of the determination of radiation distribution diagrams of antennas may be evaluated less pessimistically if functions of the type:

$$\frac{\sin\alpha}{\alpha},\ \cos^2\alpha,\ e^{-\alpha^2},\ \frac{\cos\alpha}{1-(\frac{2}{\pi}\alpha)^2},\ \frac{2J_1(\alpha)}{\alpha} \qquad [1]$$

(J_1 = Bessel function of the first order) are used. Comparing such solutions with real radiation distribution diagrams it may be said that such functions may be used for hygienic evaluation, if the width of the beam is considered to be one half of the maximal power density value. Data on the width of the beam may be found in technical documentation on radar, but such documentation must be evaluated critically. It should be stressed that uniform distribution of power density along axes of the beam is a theoretical case, rarely corresponding to the real distribution. Difficulties may be encountered particularly in the case of narrow beams.

Particular attention should be paid to the elevation of antennas which are vertically mobile. The angle of elevation influences not only the power density at a given point but also the width of the beam.

In may be said that in the case of mobile antennas it may be more convenient to evaluate hygienic conditions not on the basis of power density measured or calculated, but on the basis of the sum of energy radiated during a given time (e.g. during one day). This would correspond to the approach (6) of considering the reactions of the human organism to microwaves on the basis of a time-weighted average dose.

For hygienic evaluation purposes the reflection from earth cannot be neglected in many instances. This may be calculated if one considers a fictitious radar representing the secondary source acting as a mirror with respect to the primary source. Adequate corrections for the measured power density should be introduced taking the polarization, reflection angles, etc. into account.

The evaluation of reflections is difficult and in certain instances (2) may make the whole hygienic evaluation doubtful. Parasitic frequencies and their influence on the microwave dose should be also taken into account.

In real conditions a given point is usually irradiated from several sources simultaneously and the resulting arithmetical sum of power densities should be accepted for hygienic evaluation.

Taking all the above points into consideration, an orderly sequence of theoretical analysis, real measurements, analysis of the real existing situation and of all the factors influencing the distribution of power density from the antennas of the equipment used, may serve for elaboration of formulas for computation of data for hygienic evaluation of working conditions. Such formulas adapted to the characteristics of the radar considered in each particular instance may serve also for prediction of the hygienic conditions in the case of new installations.

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RESONANCE METHOD FOR THE DETERMINATION OF THE COMPLEX DIELECTRIC CONSTANT OF BIOLOGIC MATERIALS IN THE MICROWAVE BAND

M. Piotrowski

Military Institute of Hygiene and Epidemiology, Warsaw, Poland

Knowledge of the electric parameters of tissues is highly useful and makes it possible, among other things, to draw conclusions about propagation conditions and energy absorbed by objects placed in the electromagnetic field. From the metrological point of view, the problem resolves itself into the determination of the complex dielectric constant $\varepsilon = \varepsilon' - j\varepsilon''$ of biologic materials with a large real component ε' and an imaginary component ε'', with magnetic inductive capacity equal to the permeability of vacuum $\mu_0 = 1$.

The problem of measuring the complex dielectric constant has been solved using the resonance method, assuming that the examined substance was placed in a cuvette, the dimensions of which were smaller than the inner dimensions of the measuring cavity. Losses in the walls of the cuvette and its geometry were taken into consideration.

Difficulties typical for resonance methods and connected with materials which have high dielectric constants and at the same time great losses can be partly avoided by placing samples in a weak electric field. Such measuring conditions are guaranteed by cylindrical resonators with field distribution of quasi-H_{O11}* made where the examined substance is placed concentrically (Fig. 1).

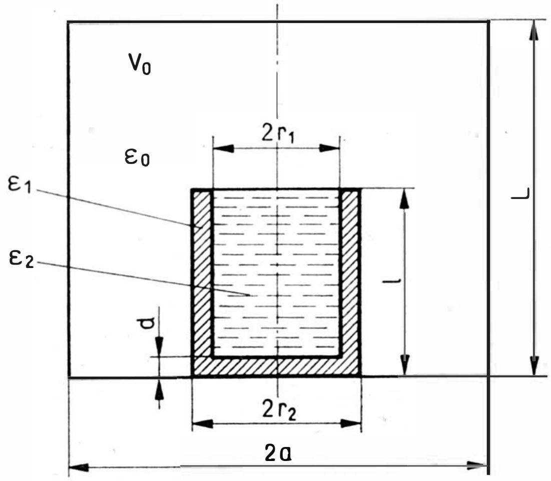

Fig. 1. Measuring cavity.

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* The definition of quasi-H_{011} is understood as a kind of free vibration of the resonator which changes into the H_{011} mode when the disturbance is removed.

Such a system makes it possible to obtain a high Q factor, easy re-tuning by contactless short-circuiting switch and large attennuation of undersirable modes. Simple technology ensures tolerances in building the cavity and in preparing samples in cuvettes for examined liquids.

There are two aspects to the realization of this task:

First — the electrodynamic aspect which may be reduced to the solution of the internal electrodynamic problem for the case of an isotropic medium described in compartments by a continuous function of dielectric permittivity of a nonhermitian symmetry (which means the occurrence of losses) filling the cavity incompletely;

Second — the metrologic aspect based on experimental determination of the resonance frequency and the Q factor of the resonator with and without a sample, and establishing interrelations linking these quantities with certain physical parameters of the resonator and the examined material.

Geometric heterogeneity and existence of losses in the examined material are the reason for difficulties in arriving at an analytical description of electromagnetic effects. The accurate solution of such a problem is not known.

So far, attempts to solve these problems by a perturbation method, as one of a number of similar general methods of analysis, have been made.

The condition of low disturbance*, which is connected with this method, has narrow limits both electric and geometric, and limits the range of application and the precision of the results obtained.

Lack of formal criteria of error evaluation makes it necessary to evaluate deviations by an indirect way estimating by approximation of disturbed fields or by experimental verification.

The problem can be solved with arbitrary accuracy by projection methods, based on an initial approximate equation and then an accurate solution of the approximate equation. Generally, approximate equations are composed in such a way that problems described by differential or integral linear operators are resolved into solving of a finite set of algebraic equations. Galerkin's method is one of the general projection methods of analysis. This method belongs to a group of methods, in which the solutions are looked for in a form of expansion into series of functions according to a complete set of functions.

In practice, Galerkin's method has been applied direct to Maxwell's equations (14). The sought field vectors $\vec{E}$, $\vec{H}$ and inductions $\vec{B}$, $\vec{D}$ were developed into series [1.1] in a complete set of self-functions obtained from solving the problem of an empty resonance cavity which has ideally conductive walls, exactly the same dimensions as the measuring resonator, and from the created electrodynamic basis.

$$\begin{aligned}
\vec{B}^N &= \mu_0 \sum_{n=1}^{N} \underline{b}_n \vec{H}_n ; \\
\vec{D}^N &= \varepsilon_0 \sum_{n=1}^{N} \underline{a}_n E_n ; \\
\vec{E}^N &= \sum_{n=1}^{N} \underline{c}_n \vec{E}_n + \sum_{n'=1}^{N'} \underline{c}_{n'} \vec{E}_{n'} ; \\
\vec{H}^N &= \sum_{n=1}^{N} \underline{d}_n \vec{H}_n + \sum_{n'=1}^{N'} \underline{d}_{n'} \vec{H}_{n'}
\end{aligned} \qquad [1.1]$$

---

* Even though Rayleigh-Schroedinger's method of disturbance calculations is not subordinated to low disturbance criteria, its utility in electrodynamics is insignificant.

Formulas for the first approximation of the theory are generally speaking less accurate than quasi-statistical approximations of the conventional theory of disturbance, and complex algorithms (sets of differential equations) are difficult to use.

Expansion factors a, b, c and d are determined by solving the matrix set of equations expressed by following algorithms:

$$\left(\Omega \underset{\wedge}{\text{Э}} \Omega \underset{\wedge}{M}\right)^{-1} \underline{b} = \frac{1}{(\omega_N)^2} \underline{b}; \qquad \text{[I]}$$

$$\left(\Omega \underset{\wedge}{M} \Omega \underset{\wedge}{\text{Э}}\right)^{-1} \underline{a} = \frac{1}{(\omega_N)^2} \underline{a}; \qquad \text{[II]}$$

$$\Omega^{-1}\left\{\check{M} - \overset{v\prime}{M}\left(\overset{\prime v\prime}{M}\right)^{-1} \overset{iv}{M}\right\} \Omega^{-1}\left\{\check{\text{Э}} - \overset{v\prime}{\text{Э}}\left(\overset{\prime v\prime}{\text{Э}}\right)^{-1} \overset{iv}{\text{Э}}\right\} C = \frac{1}{(\omega_N)^2} C \qquad \text{[III]}$$

$$\check{M} \Omega^{-1} \text{Э}\, \Omega^{-1} b = \frac{1}{(\omega_N)^2} b; \qquad \text{[IV]}$$

where:

Ω = diagonal matrix created from resonant pulsation of an empty cavity;

M = matrix describing magnetic characteristics of medium which is inside the cavity;

Э = matrix describing electric characteristics of medium and similar to matrix M made of elements in a form of scalar products;

$$\underset{\wedge}{\text{Э}}_{kn} = \varepsilon_0^2\left(\overleftrightarrow{\varepsilon}^{-1} \vec{E}_n, \vec{E}_k\right), \quad \check{\text{Э}}_{kn} = \left(\overleftrightarrow{\varepsilon}\, \vec{E}_n, \vec{E}_k\right), \qquad [1.2]$$

$$\underset{\wedge}{M}_{kn} = \mu_0^2\left(\overleftrightarrow{\mu}^{-1} \vec{H}_n, \vec{H}_k\right), \quad \check{M}_{kn} = \left(\overleftrightarrow{\mu}\, \vec{H}_n, \vec{H}_k\right).$$

In the given model of cylindrical cavity with concentrically placed sample of lossy dielectric, which is the scalar centre, given algorithms have simpler forms. In that case, matrix of M type is elementary (unitary). This is a result of the "magnetic" homogeneity of the medium placed inside the resonator ($\mu = 1$) and the arbitrary normalization. As a result of the symmetry peculiar to quasi-H_{onp} modes, only tangential components of the electric field exist in the examined sample. This means that conditions allowing the development of the electric field $\vec{E}$ in the electric sub-set of sourceless functions ($C_n = O$) hawe been fulfilled, i. e., div $\vec{E} = O$ and the normal component is continuous on the arbitrary surface inside V (with $E \in D_{div}$).

As a result, in the algorithm III used later on, besides the diagonal matrix Ω^{-1}, and the elementary matrix $\check{M}$, only matrix $\check{\text{Э}}$ is left. Also for the algorithm II, the complete basis consists of a set of rotational functions. Vector $\vec{a}$ corresponds to the expansion of induction $\vec{D}$ which for closed surfaces without source (charge) always develops in the set of sourceless functions.

After complex conversions, formulae for certain elements of matrix A describing the analysed internal problem, are obtained [1.3].

$$A c_i = \Lambda_i c_i \qquad [1.3]$$

$$\Lambda_i = \Lambda + j\Lambda'' = \frac{1}{a^2 \varepsilon_0 \mu_0 \omega_N^2}$$

In the formulae in Table 1 the indexes m, n, p mean:

m — order of Bessel's functions,

n — next element of Bessel's function,

p — visualizes field distribution along the resonator axis.

Structure of the programmed matrix is shown in Figure 2.

Eigen-value Λ i and eigen-vectors Ci of complex matrices A were calculated according to

TABLE 1
Formule

1. Diagonal words for $m = m' = 0$, $n = n'$ and $p = p'$

$$A_{ii} = \left[\mu_{on}^2 + \left(\frac{p\pi a}{L}\right)^2\right]\left\{1 + \frac{1}{J_0^2(\mu_{on})}\left[\left(\frac{1}{\varepsilon_1} - 1\right)\left(\frac{l}{L} - \frac{\sin 2\pi p \frac{l}{L}}{2\pi p}\right) I'\left(\mu_{on}\frac{r_2}{a}\right) + \right.\right.$$
$$\left.\left. + \left(\frac{1}{\varepsilon_2} - \frac{1}{\varepsilon_1}\right)\left(\frac{l}{L} - \frac{\sin 2\pi p \frac{l}{L}}{2\pi p} - \frac{d}{L} + \frac{\sin 2\pi p \frac{d}{L}}{2\pi p}\right) I'\left(\mu_{on}\frac{r_1}{a}\right)\right]\right\}$$

2. Non-diagonal words for $m = m' = 0$, $n \neq n'$ and $p = p'$

$$A_{ij} = \frac{2\left[\mu_{on}^2 + \left(\frac{p\pi a}{L}\right)^2\right]}{(\mu_{on}^2 - \mu_{on'}^2)\cdot J_0(\mu_{on})\cdot J_0(\mu_{on'})}\left[\left(\frac{1}{\varepsilon_1} - 1\right)\left(\frac{l}{L} - \frac{\sin 2\pi p \frac{l}{L}}{2\pi p}\right) I_1'\left(\mu_{on}\mu_{on'}\frac{r_2}{a}\right) + \right.$$
$$\left. + \left(\frac{1}{\varepsilon_2} - \frac{1}{\varepsilon_1}\right)\left(\frac{l}{L} - \frac{\sin 2\pi p \frac{l}{L}}{2\pi p} - \frac{d}{L} + \frac{\sin 2\pi p \frac{d}{L}}{2\pi p}\right) I_1'\left(\mu_{on}\mu_{on'}\frac{r_1}{a}\right)\right]$$

3. Non diagonal words for $m = m' = 0$, $n = n'$ and $p \neq p'$

$$A_{ij} = \frac{\mu_{on}^2 + \frac{p\pi a}{L}}{\pi J_0^2(\mu_{on})}\left\{\left(\frac{1}{\varepsilon_1} - 1\right)\left(\frac{\sin\pi(p-p')\frac{l}{L}}{p-p'} - \frac{\sin\pi(p+p')\frac{l}{L}}{p+p'}\right) I'\left(\mu_{on}\frac{r_2}{a}\right) + \right.$$
$$\left. + \left(\frac{1}{\varepsilon_2} - \frac{1}{\varepsilon_1}\right)\left[\frac{\sin\pi(p-p')\frac{d}{L}}{p-p'} - \frac{\sin\pi(p+p')\frac{l}{L}}{p+p'} - \frac{\sin\pi(p-p')\frac{d}{L}}{p-p'} + \frac{\sin\pi(p+p')\frac{d}{L}}{p+p'}\right] I'\left(\mu_{on}\frac{r_1}{a}\right)\right\}$$

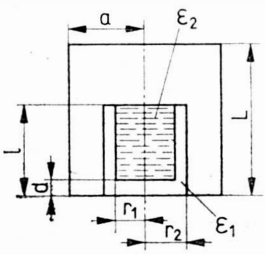
4. Non-diagonal words for $m = m' = 0$, $n \neq n'$, $p \neq p'$

$$A_{ij} = \frac{2\left[\mu_{on}^2 + \left(\frac{p\pi a}{L}\right)^2\right]}{\pi(\mu_{on}^2 - \mu_{on'}^2)\, J_0(\mu_{on})\, J_0(\mu_{on'})}\left\{\left(\frac{1}{\varepsilon_1} - 1\right)\left(\frac{\sin\pi(p-p')\frac{l}{L}}{p-p'} - \frac{\sin\pi(p+p')\frac{l}{L}}{p+p'}\right) I_1'\left(\mu_{on}\mu_{on'}\frac{r_2}{a}\right) + \right.$$
$$\left. + \left(\frac{1}{\varepsilon_2} - \frac{1}{\varepsilon_1}\right)\left(\frac{\sin\pi(p-p')\frac{l}{L}}{p-p'} - \frac{\sin\pi(p+p')\frac{l}{L}}{p+p'} - \frac{\sin\pi(p-p')\frac{d}{L}}{p-p'} + \frac{\sin\pi(p+p')\frac{d}{L}}{p+p'}\right) I_1'\left(\mu_{on}\mu_{on'}\frac{r_1}{a}\right)\right\}$$

where

$$I'\left(\mu_{on}\frac{r_{1,2}}{a}\right) = \left(\frac{r_{1,2}}{a}\right)^2\left[J_0^2\left(\mu_{on}\frac{r_{1,2}}{a}\right) + J_1^2\left(\mu_{on}\frac{r_{1,2}}{a}\right) - 2\frac{J_1\left(\mu_{on}\frac{r_{1,2}}{a}\right) J_0\left(\mu_{on}\frac{r_{1,2}}{a}\right)}{\mu_{on}\frac{r_{1,2}}{a}}\right]$$

$$I_1'\left(\mu_{on}\mu_{on'}\frac{r_{1,2}}{a}\right) = \left(\mu_{on'}\frac{r_{1,2}}{a}\right) J_1\left(\mu_{on}\frac{r_{1,2}}{a}\right) J_0\left(\mu_{on'}\frac{r_{1,2}}{a}\right) - \left(\mu_{on}\frac{r_{1,2}}{a}\right) J_1\left(\mu_{on'}\frac{r_{1,2}}{a}\right) J_0\left(\mu_{on}\frac{r_{1,2}}{a}\right)$$



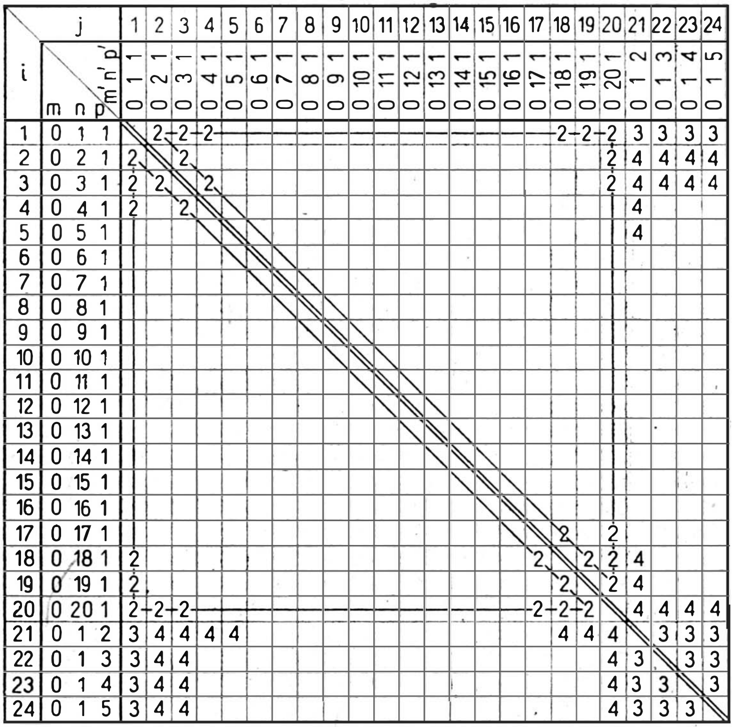


Fig. 2. Structure of matrix A.

Wielandt's method (10). The set of equations for N = 20 was solved on an Odra 1204 computer. The derived formulae are not limited and can be used for any N (size of basis). We have calculated:

1. The geometric characteristics (Fig. 3 and 4).

These show, that if the diameter of the sample increases the changes in f and Qd are bigger in comparison with the changes caused by the same gains in the height of the sample.

2. The electric characteristics f (ε'_2, ε''_2) (Fig. 5 and 6) from which, knowing from measurements the Q factor Qd, it is easy to determine ε'_2 and knowing the frequency of the resonator we can determine ε''_2 of the examined material.

EXPERIMENTAL TESTING OF DIELECTRIC PARAMETERS

The basic element of the measuring (testing) set is a resonator (Fig. 7) tunable to the X band with a field distribution H_{O11}. Two holes, symmetrically placed at the bottom of the cavity couple the resonator with the activating generator.

Coupling of the resonator with the detection set is ensured by a hole in the side of the cylinder at an angle of 45° to the axis going through the activating holes. On the inside walls of resonator, a gold layer of 10 μm has been deposed by electroplating. Measuring sets for determining the Q factor and resonator frequency are shown on Figure 8 and 9.

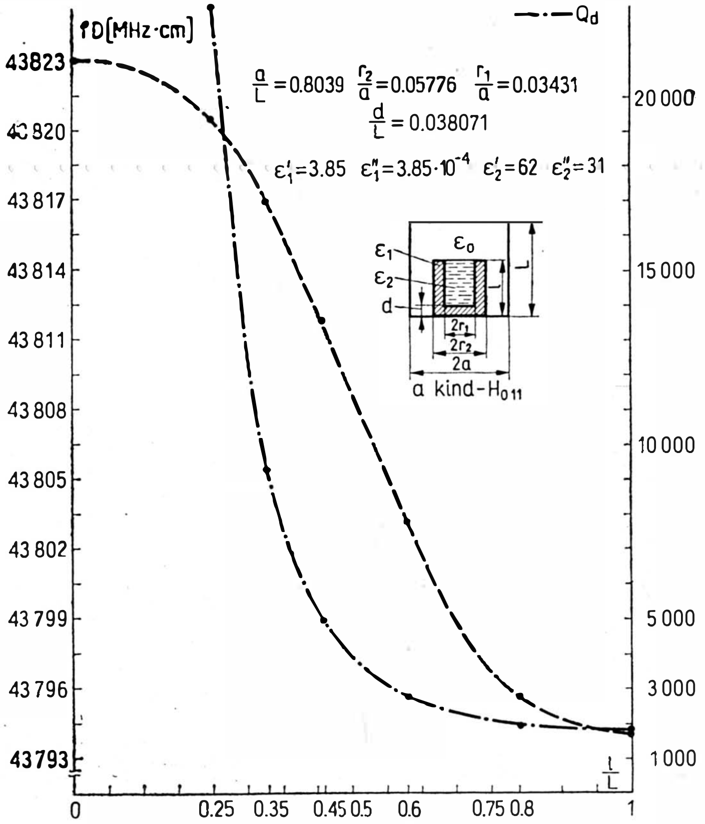


Fig. 3. Resonant frequency of H_{011} mode and Q factor conditioned only by losses in the sample as a function of the height of the sample.

Resonant frequency in band X was measured by a wavemeter Cz-3-44 (Fig. 8). Besides determining the maximum of the resonant curve by simple measurement (ensuring fine tuning accuracy $\frac{\Delta f}{f} \geqq \frac{1}{10\,Q}$) a method based on the symmetry of the resonant curve has been used, for which the fine tuning indicator eliminates the distortions (peaks) existing on peaks of the pulse output signal.

The transmission set for measuring the Q factor (Fig. 9) ensures visualization of the resonant curve on one trace of the dual trace oscilloscope and measurement of the width of the resonant curve by the use of calibration markers on the second trace.

The second trace is also, when necessary, used for controlling the generation zone of a reflex klystron with modulated frequency (GK-4-19A). Half-power level on the resonator curve was determined by introducing a 3 db attenuation through a master attenuator, X-113, into the transmission line.

Using this method, measurements of the dielectric constants of a number of biologic substances have been carried out (16). An example of the results of these measurements is shown in Table 2, together with the corresponding biologic material.

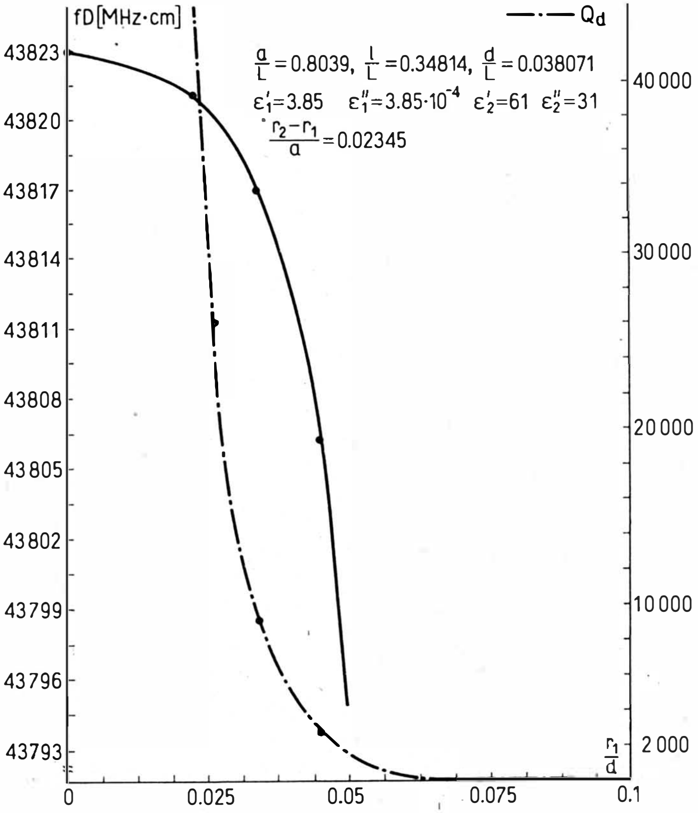


Fig. 4. The same quantities (as Fig. 3) but as a function of the diameter of the sample.

Table 2

Result

Material	Q factor of resonator with cuvette		Tuning with empty cuvette	Dielectric constant	
	Q_D	Q	Δf [kHz]	ε'_2	ε''_2
Distilled water	9650	4420	1010	61	33.5
Gamma-globulin	9650	4050	1100	66	38.0
Human blood (Na tartrate)	9650	4870	780	47	27.5

A comparison of our results with the information avilable in the literature shows agreement within the accuracy of the methods of measurement.

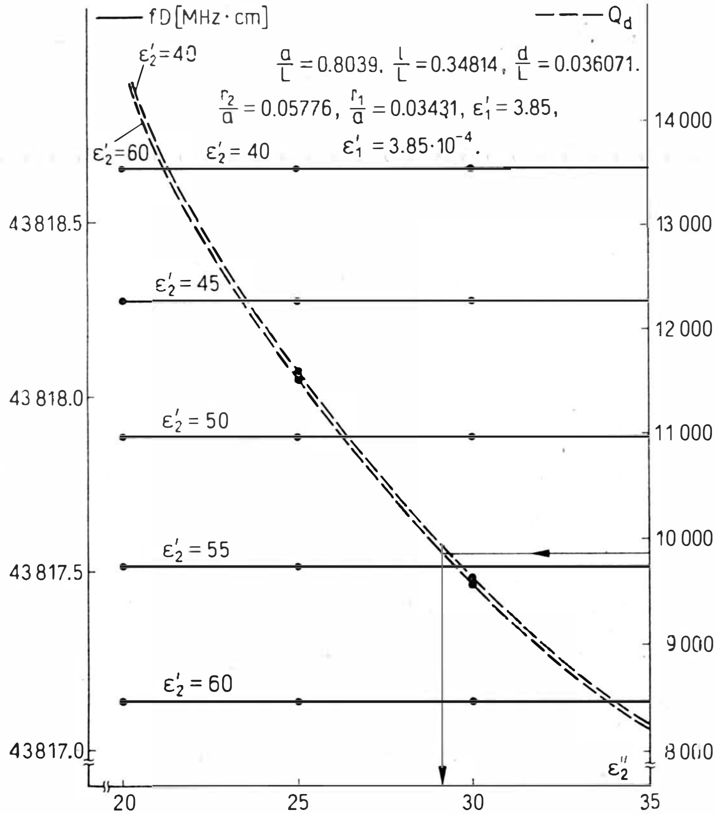


Fig. 5. Electrical characteristics.

CONCLUSIONS

Recapitulating, it is worth noting that the accurate solution of the problem is not known. Using Galerkin's method, an original solution of the problem of self vibrations of the measuring resonator has been obtained.

An analytical procedure and the use of quasi H_{onp} modes are needed for the dielectric measurement of lossy samples concentrically placed in the resonator and cuvettes, not fully filling the cavity (increasing the size of the sample to fill the cavity is a special case of the obtained dependence). There are no restrictions on size or on the material parameters of the tested substances (for isotropic media with magnetic permeability equal to vacuum permeability $\mu_o = 1$).

The characteristics mentioned here allow the choice of samples convenient for the experiment and ensure obtaining the selected sensitivity for predicted values of ε_2 and ε_1. It is evident that the most critical parameter is the inside diameter of the cuvette, for which the necessary accuracy of measurement is:

$$\frac{\Delta r_1}{r_1} \leq 1,5 \cdot 10^{-2}$$

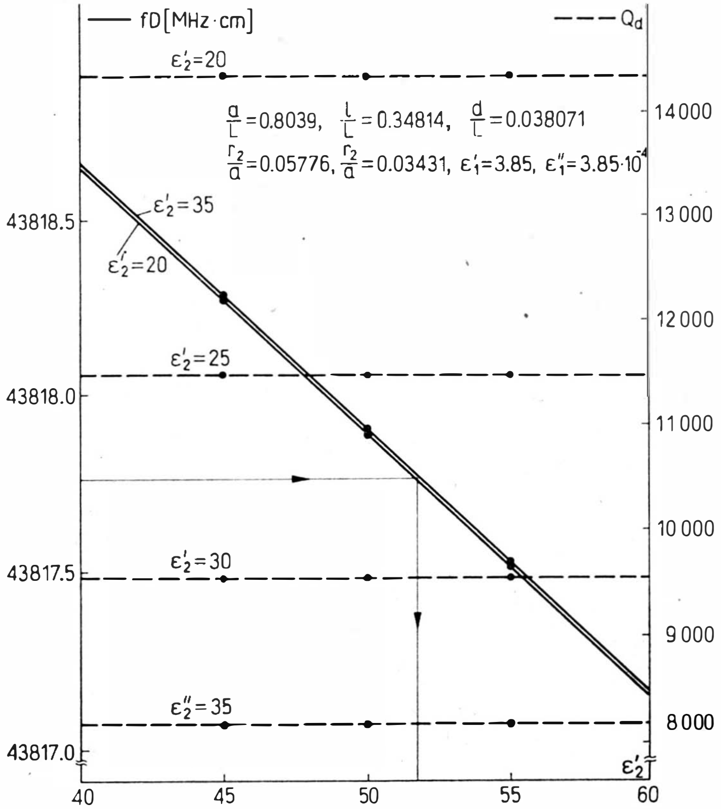


Fig. 6. Electric characteristics.

The introduction of reduced dimensions, related to the diameter of the cavity, facilitates the use of diagrams and formulae to select a range of frequencies for with the use of the resonance method is practical.

The procedure for determining the permittivity ε'_2 and ε''_2 from f (ε', ε'') and Qd (ε', ε'') may be carried out separately.

In the range of measured values $\varepsilon'_2 = (40 + 60)$ and $\varepsilon''_2 = (20 + 35)$ the error made does not exceed 0.5%. The full error in determining ε'_2 and ε''_2 is mainly due to the measuring technique used, and is (5 + 10)%.

The program worked out (16) makes it possible to introduce changes for various conditions of measuring the complex dielectric constant quickly.

* * *

Much valuable advice and many critical comments helped me to prepare this paper. I would like to thank very much all concerned and specially Prof. Dr. Ludwik Badian, Dr. Mirosław Dąbrowski and Eng. Andrzej Szubski.

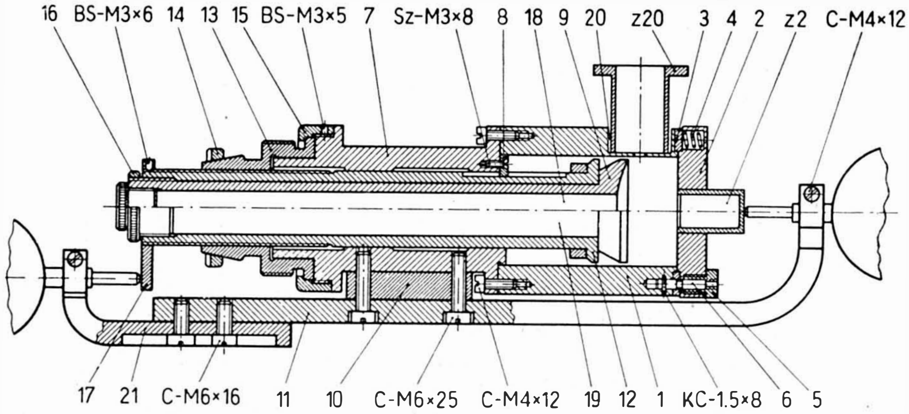

16
BS-M3×6
14
13
15
BS-M3×5
7
Sz-M3×8
8
18
9
20
z20
3
4
2
z2
C-M4×12
17
21
C-M6×16
11
10
C-M6×25
C-M4×12
19
12
1
KC-1.5×8
6
5

Fig. 7. Measuring resonator for X-band.

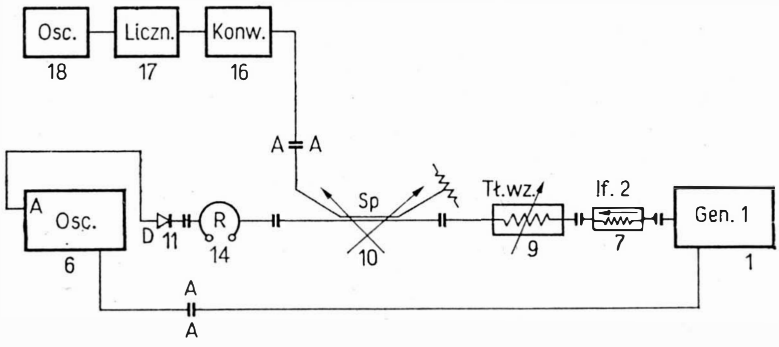

Osc.
18
Liczn.
17
Konw.
16
A
A
A
Osc.
6
D
11
R
14
Sp
10
Tł.wz.
9
If. 2
7
Gen. 1
1
A
A

Fig. 8. Block diagram of the set for measuring resonance frequency. Symbols: Gen. 1 — type GK4-19A sawtooth wobbled generator, 3 cm band, Osc. — type OKD-505A dual trace oscilloscope with time base output, If 1 — type X101A ferrite insulator, If 2 — type X103 ferrite insulator, Tł. wz. — type X130 standard attenuator. Sp. — type X121 10 dB directional coupler, D — detector, *Konw.* — type Cz4-7 frequency converter, Liczn. — type Cz3-4A frequency digital counter.

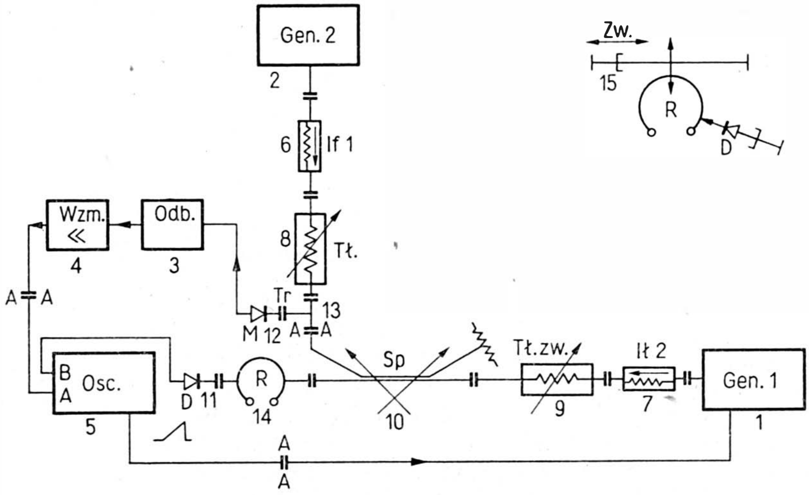


Fig. 9. Block diagram of the set for the measuring resonator band. Symbols: Gen. 1 — type GK4-19A sawtooth wobbled generator, 3 cm band, Gen. 2 — type G3-14A non-modulated generator, 3 cm band, Odb. — Type Lambda receiver, Wzm. — acoustic amplifier (own manufacture), Osc. — type OKD-505A dual trace oscilloscope with time base output, If 1 — type X101A ferrit insulator, If 2 — type X103 ferrit insulator, Tł. — type X134 non-calibrated attenuator, Tł. wz. — type X130 standard attenuator, Sp. — type X121 10 dB directional coupler, D — detector, M — mixing head, Tr. — type X153 T joint, R — the investigated resonator, Zw. — type X112 regulated contact.

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MICROWAVE REFLECTION AND DIFFRACTION BY MAN

D. E. Beischer and V. R. Reno

Naval Aerospace Medical Research Laboratory, Pensacola, Florida, U. S. A.

A study of the biologic effects of low-intensity microwave energy on man is in progress at our laboratory. To appraise the subtle effects of microwave radiation below an intensity of 10 mW/cm^2 an understanding of the fundamentals of microwave dosimetry and the use of new and improved measurement methods seemed necessary. The present investigation is specifically concerned with a study of the spatial energy distribution in proximity to man as a function of the radiation parameters. It is evident that only the field inside the body of man is relevant for judging biological radiation effects, but it is expected that valuable information contributing to the evaluation of these fields will be gained from measurements of the reflected, scattered and transmitted radiation around man. Measurements of the spatial energy distribution in proximity to man automatically take into account the complex shape and size of man and his electromagnetic as well as dynamic structure. Our approach will be to relate such measurements to similar measurements and calculations on simpler objects where the physical principles of reflection, diffraction and transmission are well understood. Since such calculations and measurements are based mostly on plane wave incident radiation, we have tried to approach this condition experimentally.

Our facility uses a large parabolic reflector (4.8 m diameter) to collimate the beam which illuminates an experimental stage (3.6 m by 3 m by 2.4 m). Any frequency between 1 and 12.4 GHz can be obtained in either continuous wave, pulsed or swept mode and in vertical or horizontal polarization. Either AM or FM modulation is available. Monochromatic radiation is assured by filtering during single-frequency operation, and multi-frequency operation is possible.

Power measurements are based on recent concepts and instrumentation developed and provided by the National Bureau of Standards (2). The high sensitivity and small size of this isotropic sensor permit very low power levels (in the μW/cm^2 range) to be measured with a high degree of spatial resolution. The energy distribution throughout the experimental space is measured by automatic scanning of a series of vertical or horizontal planes. The effects of selected objects on the pattern of the energy distribution are readily visualized by comparison of the unperturbed, incident field with the field after introduction of the object.

Figure 1 is a densigram showing the field distribution in the vicinity of man in a horizontal plane at the height of his chest. On the illuminated side a pattern of standing waves of generally parabolic shape is readily seen, and the microwave shadow region is well defined.

An attempt is made to relate these observations to a comprehensive theoretical and experimental data base concerning similar fields around inanimate objects. King and Wu (1) calculated the scattering and diffraction of electromagnetic waves by conductive and dielectric objects. Some of this information is redrawn in Figure 2 to present the field pattern for interaction of a plane wave and a conductive cylinder with axis parallel to the electric field and a cylinder diameter equal to the wavelength. The standing waves

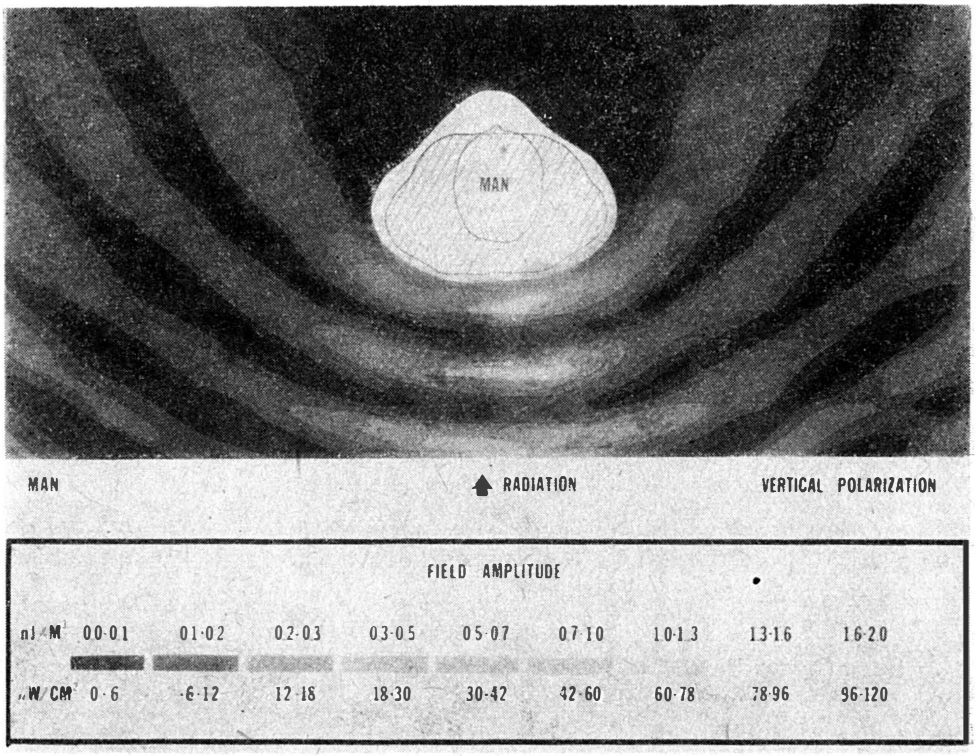

Fig. 1. Spatial energy distribution in the vicinity of man in a plane wave microwave field. 1 GHz.

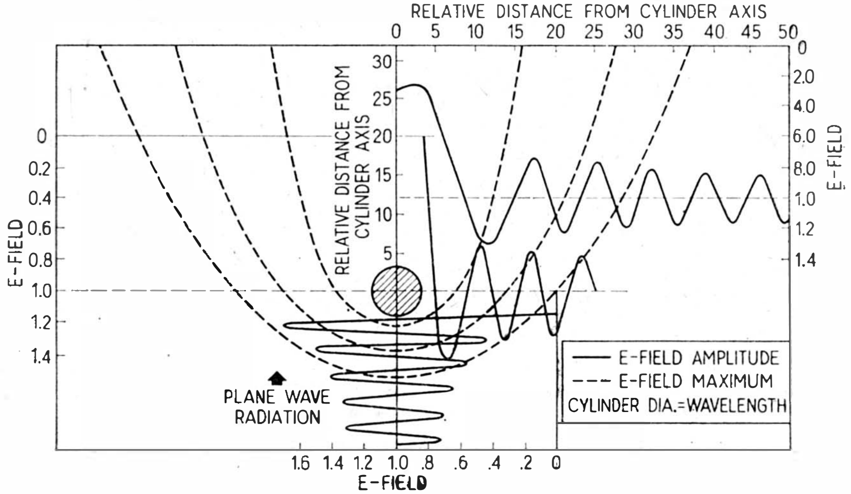

Fig. 2. Electric field near a conductive cylinder redrawn from King and Wu (1).

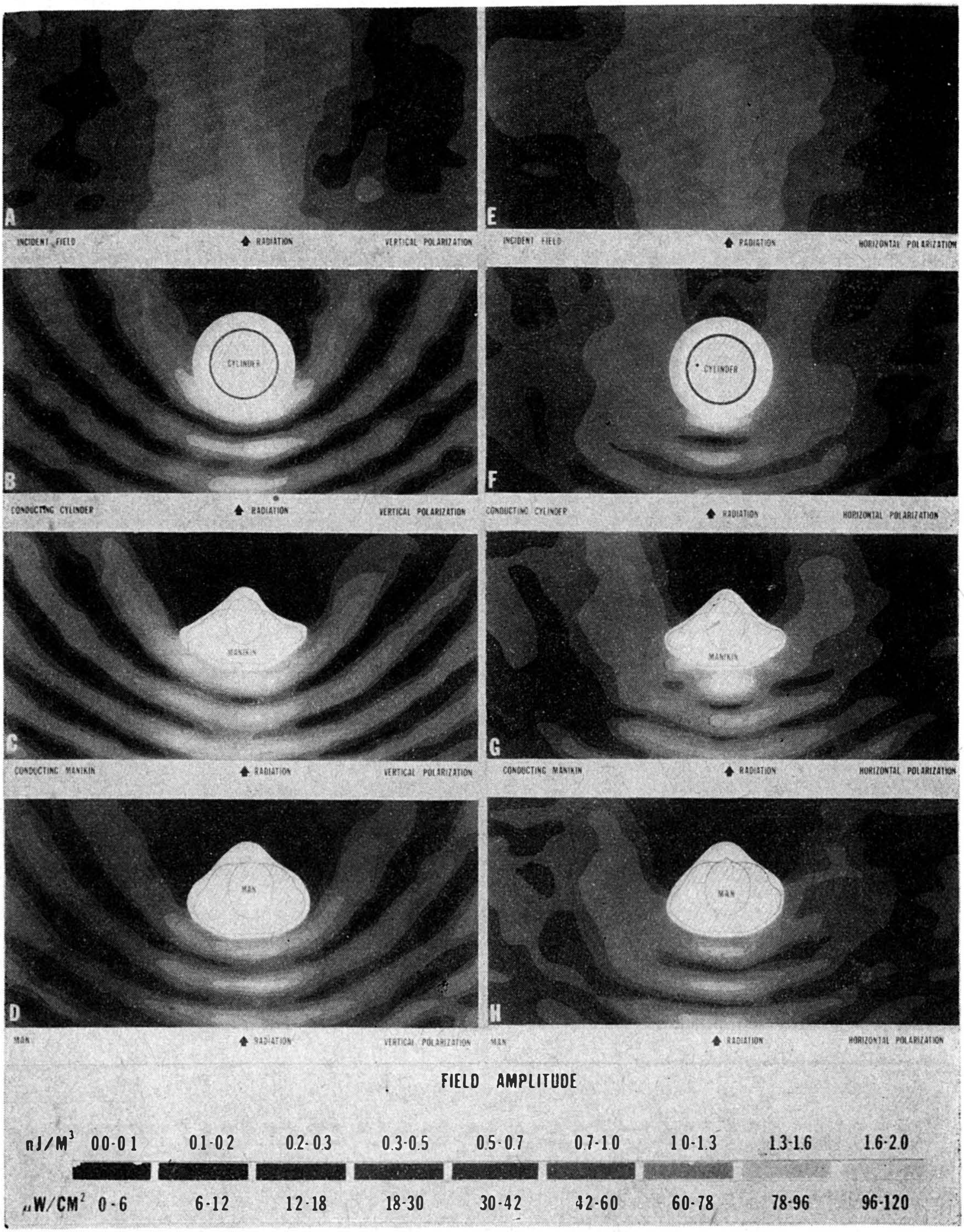

Fig. 3. Spatial energy distribution at 1 GHz (contour presentation). Row A—D Vertical polarization; Row E—H Horizontal polarization; A and E Incident field; B and F Conductive cylinder; C and G Conductive manikin; D and H man.

on the illuminated side and at two other locations are represented by dashed lines showing the parabolic curves of amplitude maxima of the electric field. These calculated curves appear similar to the pattern in Figure 1, but the shape and electrical properties of man are sufficiently different from a metal cylinder to merit special consideration. Field measurements in the vicinity of a male life-size manikin with a metallized surface were used to evaluate the influence of shape. A future comparison of the measurements on the conductive manikin with the results for a man of approximately the same shape is expected to show the influence of the electric properties of man.

Figure 3 gives a comparison of the fields measured in the vicinity of a conductive cylinder, a conductive manikin, and man for vertical and horizontal polarization and includes the incident field patterns. Figure 3 demonstrates clearly how the energy distribution is affected by the specific objects and by the polarization of the radiation. If accurate dosimetry in proximity to an object is desired, the standing wave patterns should be kept in mind. Power measurements in proximity to man for purposes of safety monitoring may be subject to gross errors in interpretation if the diffracted fields are not taken into consideration. This is true for personal dosimeters as well as for hand-held monitoring devices. Since the distance between intensity maxima in the standing wave is related to the wavelength, the positioning of the dosimeter sensor is also dependent on frequency.

The effects of polarization are easily seen in Figure 3. If the electric field is parallel to the long axis of the object (vertical polarization), the structure of the parabolic field extends a considerable distance to the side of the object, while in horizontal polarization, the side structure is low in amplitude. It can be seen that this structure is of significance if men are exposed side by side.

Curves depicting the E-field maxima calculated by King and Wu (1) for a cylinder illuminated by a plane wave and measured in our experiments with the cylinder, manikin and man are superimposed in Figure 4. The degree of correlation between the diffraction fields under the different conditions is immediately apparent. The relationship between the wavelength of the radiation and the diffraction pattern can be clearly seen on the line labeled "incident beam" where the peaks occur at intervals of one-half

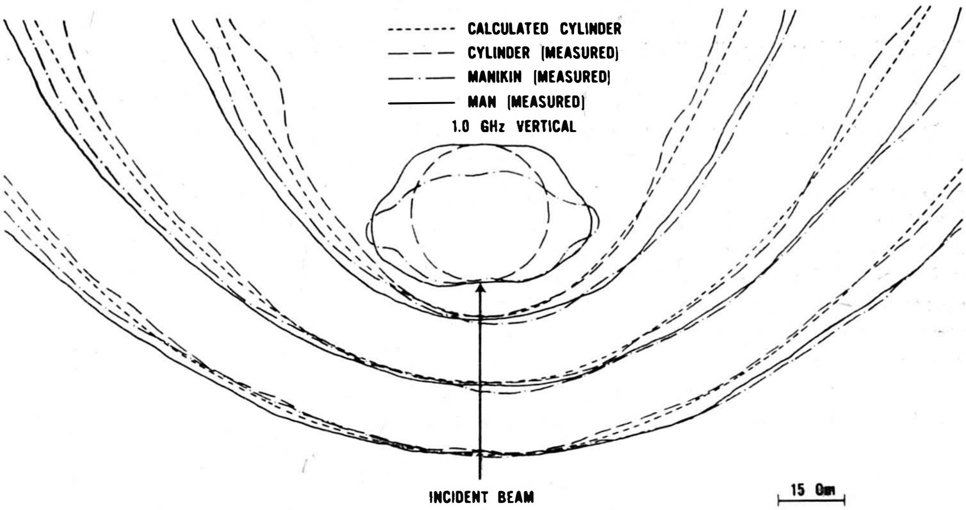

Fig. 4. Electric field maxima near diffracting objects.

wavelength. Figure 4 also shows that the effects of subject shape differences are at a minimum on the line labeled "incident beam".

A few additional observations may be of interest. The amplitude of the standing wave peaks on the beam axis diminishes with distance from the conductive cylinder and metallized manikin as is theoretically expected. If man is the scattering object, these amplitudes remain constant with distance. The difference in the two scattering patterns is best seen in A and B in Figure 5 where the information of C and D in Figure 3 is presented in a three-dimensional plot. The sagittal plane of the manikin and man is drawn in Figure 5. King and Wu (1) derived that in the case of reflection of a plane wave from an infinite, conductive plane, the amplitude of the reflected wave does not change with distance from the reflecting surface. The center of the back of man appears to act to a certain degree as an infinite conductive plane and not like a conductive cylinder. The significance of this observation has yet to be determined.

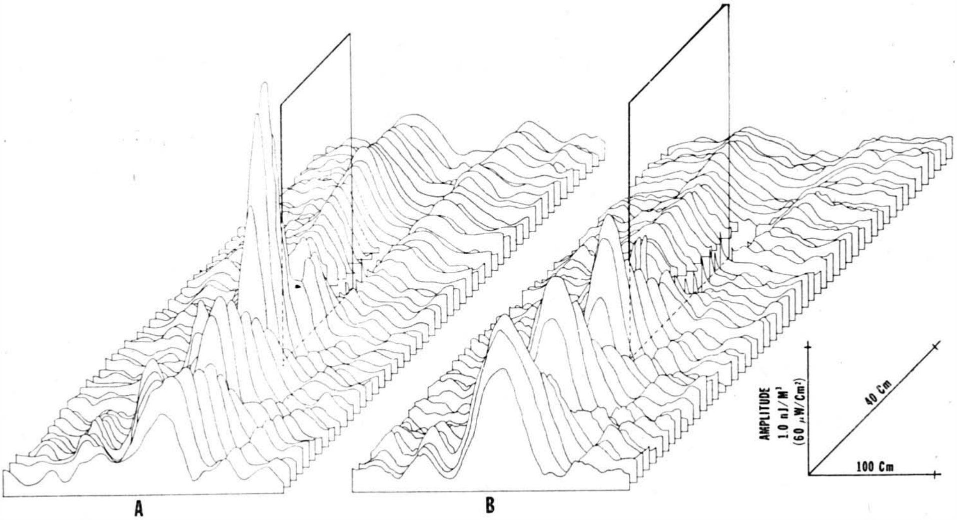

Fig. 5. Spatial energy distribution around a conducting manikin (A) and man (B). The position of the sagittal plane is indicated.

It should be pointed out in this connection that the output of the isotropic sensor at any point in space contains both phase and amplitude information about that point exactly analogous to that contained in an optical hologram. In the near future we hope to furnish additional information on the absorption of microwave energy by man by a judicious application of microwave holographic techniques.

It should be emphasized that all the studies described here, as well as others currently underway, are based upon direct measurements on human subjects. The high sensitivity of the instrumentation permits measurements to be made at the very low power levels accepted as safe for exposure of the general population. It is our belief that this approach will provide information concerning the interaction of man with a microwave environment that can be obtained by no other presently available method. In the limited space available we could indicate only the potentialities of an approach which may provide the basis for a non-invasive method to estimate the energy actually absorbed from an incident microwave field by different body parts and tissue layers of man.

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Session E. Occupational Exposure and Public Health Aspects of Microwave Radiation

Chairman: *E. Klimková-Deutschová*
Vice-Chairman: *B. Tengroth*
Rapporteurs: *Z. Edelwejn* and *R. L. Elder*

CLINICAL MANIFESTATIONS OF REACTIONS TO MICROWAVE IRRADIATION IN VARIOUS OCCUPATIONAL GROUPS

M. N. Sadčikova

Labor Order the Red Banner Institute for Scientific Research on Institute of Industrial Hygiene and Occupational Diseases, Academy of Medical Sciences of the USSR, Moscow, USSR

Studies on the biological action of microwaves have been widely conducted in the USSR over the past 20 years. The investigations have been devoted mainly to hygienic, experimental, clinical and ecological aspects of the problem. Studies are being performed in the USA, Poland, Czechoslovakia, and in Western Europe (21, 22, 23, 24).

Results of our own clinical observations of many years, as well as literature data (2, 5, 6, 9, 12, 18, 22, 23) show that, as a consequence of prolonged work involving exposure to microwaves, changes take place in the functions of the nervous, cardiovascular and other systems of the organism leading to a characteristic complex of symptoms. A distinct form of occupational disease — microwave or radiowave sickness — has been identified as a nosologic entity.

However, up till now, numerous questions concerning the clinical course and pathogenesis of certain lesions have been insufficiently elucidated.

The present communication presents clinical observations on the health status in two groups of workers engaged in the regulation, tuning and testing of diverse radioequipment emitting radiation in the microwave range.

Both groups were comparable with respect to sex and age, but differed in intensity of exposure and duration of work. Young men with a long (5—15 years) history of employment with microwave sources predominated in both groups. Those in the first group (1000) were subject to the influence of a power density of up to a few mW/cm^2. The second group (180) comprised people exposed to microwaves at lower intensities, which as a rule did not exceed several hundredths of a mW/cm^2. More significant exposure could have taken place during extremely short periods.

Some nervous tension during work could not be excluded. A group of people (200), matched with respect to sex, age and character of work processes which did not involve exposure to microwaves, served as a control.

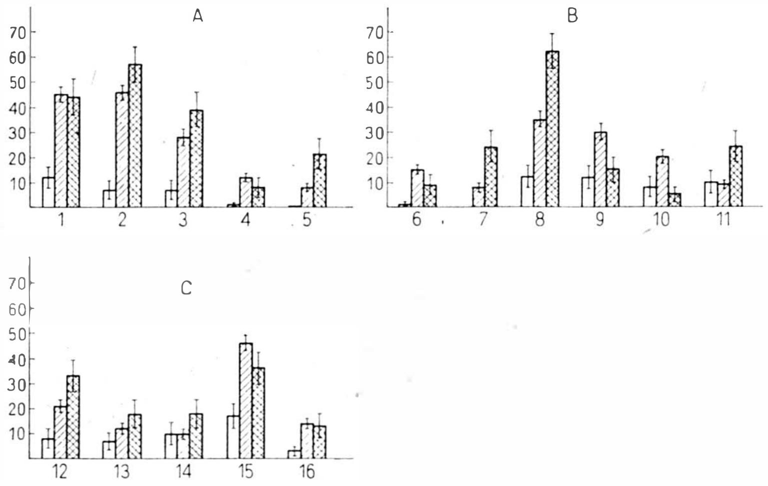

Fig. 1. Changes in the nervous and cardiovascular systems among workers exposed to microwaves and control subjects. Ordinate — frequency of changes in percentages; abscissa — main indicators: A — neurological, B — autonomic vascular and C — cardiac. White columns — control; oblique shading — persons of the first group, exposed previously to periodic action of microwaves of substantial intensities; double shading — persons of the second group working under conditions of exposure to microwaves of lower intensities. All indicators are presented with confidence limits. 1 — feeling of heaviness in the head, 2 — tiredness, 3 — irritability, 4 — sleepiness, 5 — partial loss of memory, 6 — inhibited dermographism, 7 — expressed dermographism, 8 — hyperhidrosis, 9 — bradycardia (upon counting), 10 — arterial hypotension, 11 — arterial hypertension, 12 — cardiac pain, 13 — dullness of the heart sounds, 14 — systolic murmur, 15 — bradycardia (according to ECG), 16 — lowering of deflections T I and T II.

Figures 1 and 2 show the frequency of the main subjective and objective changes in the subjects examined, as well as the relationship of these changes to duration of work under given conditions.

Inspection of Figure 1 shows that people of the first and second group significantly differed from the control in frequency of such complaints as heaviness in the head, tiredness, irritability, drowsiness during the day, anxiety and light sleep at night and partial loss of memory. In both groups attention was drawn to various autonomic vascular changes: inhibited or expressed dermographism, hyperhidrosis of the hands, instability of pulse and arterial pressure increasing during functional loading (orthoclinostatic test, Aschner's test, graded physical loading), tendency to bradycardia (pulse rate of up to 60 per min) and arterial hypotension (systolic pressure of up to 100 mm Hg) or hypertension (systolic pressure of more than 135 mm Hg) appearing against the background of normal arterial pressure and accompanied by narrowing of retinal arteries (1).

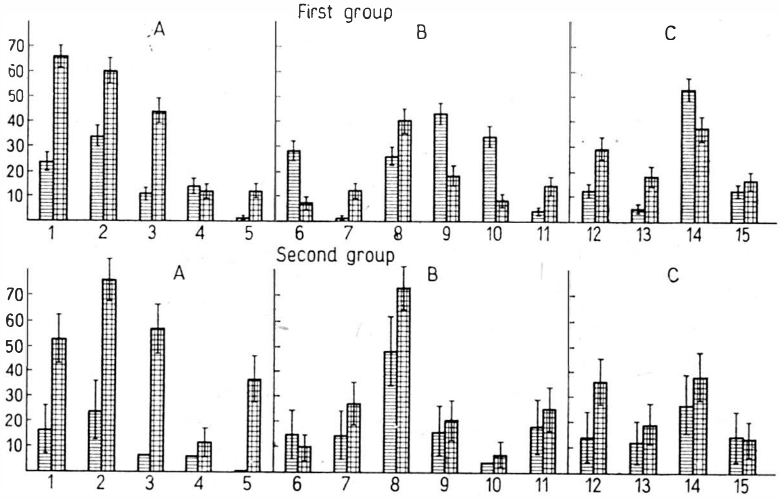

Fig. 2. Changes in the nervous and cardiovascular systems among those under 40 with varying duration of work involving exposure to microwave irradiation. Ordinate — frequency of changes in percentages, abscissa — main indicators: A — neurological, B — autonomic vascular and C — cardiac. Horizontal shading — duration of employment of less than 5 years; double shading — duration of employment of 5—10 years. First group — persons exposed previously to periodic exposure to microwaves of substantial intensities; second group — those working under conditions of exposure to microwaves of lower intensities. All indicators are presented with confidence limits. 1 — feeling of heaviness in the head, 2 — tiredness, 3 — irritability, 4 — sleepiness, 5 — partial loss of memory, 6 — inhibited dermographism, 7 — expressed dermographism, 8 — hyperhidrosis, 9 — bradycardia (upon counting), 10 — arterial hypotension, 11 — arterial hypertension, 12 — cardiac pain, 13 — dullness of the heart sounds, 14 — bradycardia (according to the ECG), 15 — lowering of deflections T I and T II.

Functional thyroid changes with increase of its activity occurred not infrequently (15).

Predominant complaints concerned cardiac pain of a lancinating or boring, and less frequently constricting, character radiating to the scapula and arm. The heart sounds were dull and functional systolic murmur over the heart apex was present.

Electrocardiographic examination revealed minor disturbances of intraventricular conduction (conduction of the initial part of the ventricular complex amounted to 0.10 s or 0.11 s and more), sinus bradycardia and moderate lowering of T deflection in standard leads. In some cases more pronounced changes of T deflection were observed (lowered, smoothed or negative T deflection) in left chest leads, accompanied by minor downward displacement of the S—T segment without conspicuous changes in its shape, and by increased duration of electric ventricular systole. In a number of cases these changes in T deflection were combined with bradycardia and deceleration of intraventricular conduction which, taken together with complaints of heart pain and hypertensive reactions, led to their being taken for myocardial lesions or manifestations of coronary spasm (4, 12).

Autonomic vascular changes in persons of the first group exposed periodically in the past to microwaves of high intensities had vagotonic, as well as sympathicotonic, character, while in the second group they were predominantly sympathicotonic.

In both groups (Fig. 2) the frequency of asthenic and autonomic vascular disturbances of a hyperreactive character (expressed dermographism, hyperhidrosis, arterial hypertension) related to age and employment depended directly on the duration of professional contact. Among those working for 5—10 years reactions of this type predominated in the second group, but they were more pronounced in the first one. As to vagotonic reactions (inhibited dermographism, bradycardia, arterial hypotension), they occurred mainly in the first group in the initial period of work with microwave sources.

The above data showed that microwave action was characterized by autonomic vascular symptoms of a vagotonic character. At the same time the symptoms of dystonia of the hypertonic type, related to nonspecific regulatory shifts, were less clearly related to intensity of action. Their etiology and clinical significance require further verification.

Only minor changes were found in the peripheral blood in both groups (16, 17). Some decrease in mean erythrocyte count was found (4 600 000 ± 0.18 and 4 600 000 ± 0.031 in the first and second group, respectively), as compared with controls (4 700 000 ± 0.17). Slight thrombocytopenia occurred in the first (221 500 ± 2.53) and second (216 300 ± 4.13) groups; controls: 245 000 ± 1.6. Moderate leukopenia was found in the first group (5 930 ± 0.065); controls: 6 490 ± 0.058. In a number of cases leukocytosis was encountered in the initial period of professional contact.

A tendency to cytopenia was observed predominantly in the first group with longer duration of employment. These people showed signs of a qualitative deterioration of erythrocytes, with a tendency to spherocytosis and an increase in acid fragility. Decreased numbers of mature cells of the neutrophilic series and signs of stimulated erythropoiesis were noted in bone marrow smears. Examination of ordinary bone marrow smears and of metaphase plates did not reveal an increased frequency of chromosome aberrations by comparison with controls.

Examination of deep refracting media of the eye revealed opacities of the crystalline lens as viewed in the slit lamp (1). Opacities were distributed mainly in the cortical layer and in superficial layers of the mature nucleus along its equator, and only single ones were found in the centre. Their frequency did not exceed control values. However, with increasing duration of occupational exposure the opacities of the lenses progressed. In a few cases the subjects of the first group workin gin unfavourable conditions developed cataracts with opacities of the crystalline lens detectable even in transmitted light.

In the majority of those examined single abnormalities in their health status did not interfere with the usual rhythm of life and work.

In a number of cases the abnormalities combined into a complex of symptoms which required therapeutic intervention.

Upon close examination in the ward a complex of symptoms corresponding to microwave sickness was diagnosed only in those patients of the first group who began their work under the most unfavourable conditions. Its frequency in the whole group did not exceed 15%.

We showed previously (4, 7, 13) that the clinical picture of microwave sickness was characterized by a complex of various autonomic vascular disturbances with crises of cerebral and coronary vascular insufficiency and asthenic symptoms. We distinguished three stages in the development of the sickness according to criteria generally accepted by pathologists: initial (I), moderately advanced (II) and advanced (III) with the following main clinical syndromes: asthenic, astheno-autonomic with vascular dysfunction of hypertonic type, and hypothalamic (autonomic vascular form).

The asthenic syndrome occurred in the initial stages of the disease. It included mainly a complex of asthenic symptoms dominated by autonomic vascular changes with a vagotonic tendency.

The syndrome as a whole took a benign course.

The astheno-autonomic syndrome with vascular dysfunction of the hypertonic type was most frequent and occurred largely in moderately advanced and advanced stages of the disease.

In the clinical picture of a given syndrome, with the background of deepened asthenic phenomena, of primary importance were the autonomic disturbances related to increased excitability of the sympathetic division of the autonomic nervous system as well as vascular instability with hypertensive and angiospastic reactions. The latter frequently determined the severity of the illness.

At a certain stage of development of autonomic vascular disturbances the hypothalamic syndrome (autonomic vascular form) appeared and was characterized by sudden crises, predominantly of a sympathico-adrenal character.

The astheno-autonomic and hypothalamic syndromes took a protracted course. In advanced stages of the disease the asthenic, emotional and autonomic vascular disturbances and crises became more pronounced. In a number of patients the clinical picture of ischaemic heart disease and hypertension developed; the latter was frequently of the cerebral type.

Angiospastic symptoms were confirmed by the results of rheographic examinations of brain hemodynamics which showed a lowered intensity of pulse blood flow and predominantly an increased tonus of intra- and extracranial vessels which was restored under the influence of the nitroglycerine test (14).

Data of mechanocardiographic investigations showed increased tension-relaxation changes of vessels of the muscular type and increased peripheral resistance (4, 11).

Similar changes in the cardiovascular system were observed by a number of investigators (8, 10, 19, 20).

Electrocardiographic changes (3) and abnormal findings in some biochemical tests (13) correlated with the clinical observations.

In the initial stages of the disease electroencephalograms of the patients disclosed changes in alpha activity, stable alpha rhythm or decreased amplitude of alpha waves. In moderately advanced and advanced stages, bilateral synchronous discharges of theta- and delta-waves were found, and sometimes diffuse slow oscillations most clearly seen on hyperventilation, thus showing that subcortical structures were involved in the pathological process.

In the early period changes in protein composition took place, as evident from increase in total serum proteins, dysproteinemia and lowered albumin-globulin ratio.

Changes in the sugar curve after glucose loading — flattening (1st type), so-called diabetic (2nd) type, sometimes of biphasic character — accompanied all clinical forms of the disease, but they predominated in neurocirculatory disturbances with crices.

Some increase in cholesterol level, lowered lecithin-cholesterol ratio and decrease in blood chlorides were seen. Some authors (8, 10) have reported dysproteinemia, dyselectrolytemia and changes in blood lipid levels.

In moderately advanced and advanced stages of the disease catecholamine excretion was changed and the epinephrine-norepinephrine ratio was lowered, although the content of these amines in daily urine collections was normal. A few patients during crises exhibited sharp fluctuations of epinephrine levels, as well as an unusual daily rhythm of norepinephrine, excretion, the latter characterized by increase in the evening and at night.

Certain abnormalities in glucocorticoid metabolism were found: the overall index was lowered and the ratios of discrete fractions were changed. Changes in catecholamine excretion and in metabolism of glucocorticoid hormones were more marked after epinephrine loading which led to development of clinical autonomic vascular reactions.

The above investigations confirmed the clinical and electroencephalographic observations showing that deep, and particularly hypothalamic, structures of the brain were involved in pathological processes. Dysfunction of the hypothalamus, hypophysis and suprarenals, appearing against a background of asthenic phenomena, could be of importance in the pathogenetic mechanisms of development of the clinical symptoms of microwave sickness.

Investigations (Tab. 1) of those patients suffering from microwave sickness of one to ten years' duration (3—6 years in the majority of cases) showed that, despite repeated therapeutic courses and temporary withdrawal from work with microwave sources, upon returning to previous work conditions symptoms increased in severity, particularly among patients with moderately advanced and advanced stages of the disease. In such patients autonomic vascular disturbances dominated, crises of cerebral and coronary insufficiency progressed and development of ischaemic heart disease and hypertension was observed.

Table 1

Clinical course of microwave radiation sickness during and after exposure

Clinical syndromes	Period of observation*	No. of cases	Clinical course**		
			Recovery	Stabilization	Progression
Asthenic	A	24	—	13 54±10	11 47±10
	B	5	3 60±24	2 40±24	—
Astheno-autonomic with vascular dysfunction	A	47	—	—	47 100±2
	B	16	—	15 94±6	1 6±6
Hypothalamic (autonomic vascular form)	A	2	—	—	2 100
	B	6	—	5 83±17	1 17±17
Total		100	3 3±2	35 35±5	62 62±5

* A — during employment under conditions of microwave exposure
B — after cessation of exposure to microwaves
** Above, number of cases; below, percentage ± S.E.

Cessation of work involving irradiation frequently resulted in stabilization of the processes, or even recovery, if withdraval took place in the initial stage of the illness

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NEUROLOGIC FINDINGS IN PERSONS EXPOSED TO MICROWAVES

E. Klimková-Deutschová

Neurologic Clinic, Charles University, Prague, Czechoslovakia

Twenty years ago, when I started the systematic examination of persons occupationally exposed to electromagnetic fields, no detailed neurologic findings had been reported in the literature. At that time, no instruments were available for making precise measurements of field intensity values. There was also a lack of other technical information, for example concerning the absorption of energy within the organism. Much later, however, special departments were established in the Institute of Industrial Hygiene for research work on the hazards of electromagnetic waves and it took several more years before instructions were published regarding preventive measures and measurements.

Our first experimental findings in people occupationally exposed to electromagnetic fields were confirmed by other investigators. This applied especially to changes in EEG recordings, which were observed even under rigorously controlled experimental conditions, using precise intensities and frequencies.

Depending upon the frequency with which the neurologic findings deviated from normal in groups observed at different places of work, it was possible for us to differentiate various levels of hazard in the working environment even before we knew the precise exposure intensities. In my previous work, I was able to show that there were significant clinical and electrobiologic changes in exposed persons as compared with controls. I distinguished three main stages in the clinical picture, based on the signs and symptoms observed. In agreement with the clinical and EEG findings, the results of biochemical studies on selected groups exposed to radiation in the centimeter band could be interpreted as dependent on an impairment of central nervous regulatory mechanisms.

I introduced into the neurologic examination the detailed investigation of the extrapyramidal system, making use of the contralateral responses to cerebellar and extrapyramidal disturbances. Using a refined test battery of cerebellar functions, we were able to interpret the phenomena corresponding to cerebellar irritation as extrapyramidal signs, e.g. hypotonus as opposed to hypertonus. Together with other motor disturbances these were the earliest manifestations of organic microsymptoms, even in persons without subjective complaints.

By making an exact evaluation of the extent of the disturbances, we were able to estimate that most of our patients had suffered less serious injury than had some other groups working with chemical noxious agents. In several papers, I discussed the possible pathophysiology of the nervous system damage on the basis of thermal or non-thermal effects.

A special feature of our results lies in the fact that when the investigations were started preventive measures were not strictly observed and less attention was paid to the hazards than is the case today. Nowadays, strict hygienic supervision of working places prevents the development of serious organic injury. Our previous results provide useful evidence of the nature of the lesions that can develop.

MATERIALS AND METHODS

We have made repeated observations on 530 persons occupationally exposed to non--ionizing radiation, so that we have at our disposal more than 1000 findings. We succeeded in compiling data from 29 places of work. In view of the variability of the material, I attempted to undertake a computer analysis of a selected sample of 352 detailed case histories on the basis of 119 parameters. The most homogeneous groups consisted of 162 workers who were exposed to radiation of centimeter wavelengths. The other groups were used for comparison.

Among the parameters studied were: age, characteristics of exposure, constitutional factors, non-specific influences unconnected with occupation, clinical signs and symptoms, EEG findings, and biochemical changes. On the basis of the computer analysis, the subjects studied may be divided into 8 groups:

1. Workers engaged in metal welding, exposed to frequencies ranging from 0.5 MHz up to 3.5 — 32 MHz.
2. Workers from two steel factories engaged in tempering steel and exposed to frequencies of 0.45—150 MHz, with a daily exposure of 50—112 V/m, and occasionally 400 V/m.
3. Welders of plastics: frequency range 12—150 MHz, daily exposure 20—57.7 V/m.
4. Technicians operating television transmitters.
5. Workers at a radio transmitting station operating at a wide range of frequencies, from 6 MHz up to 30 MHz, and using a pulsed field system.
6. Persons exposed to radiation in the 3—13 cm wave-band working in industry and at research institutes with frequencies ranging from 3 GHz to 30 GHz. Intensity measurements showed permissible levels in some places, but in others values exceeding the permissible level ten or more times were found.
7. Persons working on a linear particle accelerator.
8. A mixed group which included the administrative staffs of two factories, who were not directly exposed to non-ionizing radiation, some workers with exposures of less than 300 MHz and others with exposures of 300—800 MHz.

Symptoms were found most frequently in workers exposed to radiation in the centimeter wave-band. The occurrence of such symptoms as headache, fatigue, and excitability was statistically significant, while the frequency of anxiety and some other symptoms was not significant. In nearly all the groups, fatigue was noted more often than excitability, statistically significant differences being again found in workers exposed to centimeter wavelengths.

Subjective complaints were even more frequent in group 5, who were mainly exposed to a pulsed field. As regards objective signs, there was a statistically significant increase in the frequency of signs of autonomic nervous system disturbances in groups 5 and 6 and cerebellar symptoms appeared in group 6. Signs attributable to the extrapyamidal system were observed in groups 1, 2 and 6, but the frequency was significant only at the 5 percent level, while in groups 2 and 6 the frequency of signs attributable to the pyramidal system was significant at the 1 percent level.

Age played no significant role in the frequency of symptoms. In our computer analysis, only people below 30 years of age showed a significantly higher incidence of autonomic disorders. Physiologic impairment of the autonomic nervous system played a role in young persons. In the fourth decade, a raised diastolic blood pressure, significant at the 1 percent level, was found in 51 percent of our subjects. Only limnal changes were found in the EEG between the ages of 20 and 40 years, and blood pressure was normal in the second and fifth decades. Intracranial arachnitis was present in the fourth decade, the frequency being significant at the 5 per cent level. Memory disturbances were seen in persons over 50 years of age. Most of the parameters studied were not significantly correlated with age. It can be assumed that, as a rule, there is practically no dependence on age as far as symptomatology is concerned. Measurements of the temperature of the cerebrospinal fluid showed maximal values in the cisterna magna. The incidence of cerebellar signs may thus be explained by the heating effect in the posterior fossae.

ELECTROENCEPHALOGRAPHIC EXAMINATION

In agreement with the subjective complaints of fatigue, we found a reduction in vigilance in 59 percent of persons exposed to radiation in the centimeter band. A predominance of inhibitory processes was proved not only by the EEG findings but also by use of the conditioned reflex method of examination. In addition to subclinical activity, pathological findings in the EEG recordings included pointed synchronized waves of high amplitude and slowed rhythms. Synchronized activity as a proof of functional disturbance of the CNS could be seen even in recordings showing limnal changes. Such activity was present in 14.3 percent of persons in group 5 and can be explained by the involvement of midline structures. It must be emphasized that in most instances the alterations in the EEG were only very slight, appearing most frequently after activation by hyperventilation. The EEG offers an important objective method of examination at a time when clinical evidence of disordered function — in particular neurotic signs — is only slight. The EEG findings are often more important than the clinical ones. EEG examination makes it possible to reach conclusions about the prognosis for the patient and about a suitable assignment of work.

BIOCHEMICAL STUDIES

Biochemical studies on a group of 40 persons exposed to radiation in the centimeter band included the determination of the levels of pyruvic acid and lactic acid in the serum and of creatinine in the urine. In the majority of persons all three metabolites showed normal levels, but there were twice as many with decreased values as with increased values. We also found some abnormalities in the blood sugar curve, with a slight increase in the fasting blood sugar in about 74 percent of cases. A few persons showed a flat or prediabetic type of curve, with slight glycosuria.

In persons exposed to radiation in the 30—800 MHz range, we studied the serum protein levels and the levels of cholesterol and lipoproteins. Serum protein levels were found to be raised in 75 percent of subjects with an average age of 45.5 years. Raised beta-lipoprotein levels were found more than twice as frequently in exposed workers as in controls. Cholesterol levels were elevated in 40.9 percent of the exposed subjects, but in only 9.5 percent of the controls. These data are in agreement with those previously reported in the literature.

DISCUSSION

The quantity of creatinine excreted during 24 hours is practically constant in any individual, but it depends on the total muscle content of the body and on muscular activity. Fever, starvation, irradiation by waves shorter than the visible part of the spectrum, and catabolic processes accompanied by destruction of muscle all raise the level of creatinine in the urine. On the other hand, in our series creatinine levels were more often decreased than increased. We can only attribute this to a disturbed regulation of creatinine excretion in 60 percent of cases.

The increased levels of fasting blood sugar and the variations in pyruvic acid and lactic acid levels, together with the anomalies in creatinine excretion, point to slight disturbances in enzyme functions. The most constant observation was the slight increase in fasting blood sugar. A similar increase is observed in cases of hypertension and arteriosclerosis and in nervous system involvement accompanied by altered glucose tolerance. In the light of these findings, hypolacticemia may be interpreted as evidence of a tendency to acidosis. It is also of interest that in our earlier studies we observed a statistically significant increase in the incidence of hypertension, particularly in the third decade, as compared with that reported by Böger and Wetzler in a large survey undertaken for American insurance companies.

In contrast to the values determined in persons subjected to experimental sleep deprivation, in our cases we found that decreased levels of the metabolites mentioned occurred twice as often as increased ones. It is known that heat by itself changes the relative concentrations of the protein fractions in the blood serum, causing especially an increase in the gamma fraction.

The reduction in vigilance and the pathologic changes in the EEG were attributed to a diminution in afferent stimuli from the reticular formation in the brain stem. From the metabolic disurbances, the EEG changes, and the clinical signs and symptoms, it may be concluded that the impairment of regulatory mechanisms is localized in the mesodiencephalic region. The focal, temporal and brain stem lesions may be explained by the rectangular branching of the vessels in these parts of the brain. The heating effect is a consequence of the poor efficiency of the cooling by the blood stream. However, the involvement of midline structures in persons exposed to certain wavelengths may be presumed to be due to a direct influence of the radiation.

One consequence of the heating effect is, however, a rise in basal metabolism, which could increase the oxygen requirement of the tissues. The rise in temperature may also reduce the oxygen-carrying power of the hemoglobin, causing decreased oxygenation, and lead to respiratory alkalosis. This metabolic effect could explain the pathologic changes in EEG activity, with subclinical episodic rhythms similar to those seen in epileptic seizures. Studies made by Lawrence on irradiated skin have also shown that tissue activity is decreased under the influence of electromagnetic waves. The EEG disturbances may also be explained on a non-thermal basis as the result of direct stimulation; they may even be provoked by nociceptive stimulation of the skin.

It is well known that non-thermal effects of irradiation have been demonstrated by the induction of mutations in some primitive organisms and by the ability of such organisms to sense the presence of weak electric and magnetic fields. A non-thermal origin is also assumed for the effects on endocrine organs, changes in membrane permeability, and chromosome aberrations.

Molecular resonance, the splitting off of free radicals, and the interruption of enzymatic chain processes leading to disturbances in fine regulatory mechanisms are possible ways in which electromagnetic waves may influence living organisms. Such mechanisms would explain the alterations in tissues with high enzymatic activity and a high oxygen requirement. The distribution of energy also depends on the conducting and reflecting properties of the tissues.

CONCLUSIONS

1. By means of computer analysis, a qualitative and quantitative evaluation was made of the data obtained on 352 persons in regard to clinical, biochemical and bioelectric signs, and their dependence on age and the characteristics of the exposure to electromagnetic radiation.

2. Our results confirm our earlier conclusion that the disturbances of the nervous system may be divided into three main stages:

(a) the neurasthenic syndrome with autonomic disorders,

(b) pseudoneurasthenia with similar subjective complaints, but with microsymptoms of an organic nature, especially in motor systems,

(c) very rare cases of encephalopathy.

3. The occurrence of contralateral responses to cerebellar and extrapyamidal disturbances facilitates the detection of early signs of extrapyramidal syndromes, which are identical with those caused by cerebellar irritation.

4. The predominance of fatigue in certain of the exposed groups was paralleled by a reduction in vigilance, as noted in the EEG recordings and in our earlier studies of higher nervous functions.

5. The occurrence of synchronized EEG activity, with slow rhythms of high amplitude similar to those seen in epileptic seizures, taken in conjunction with the clinical and biochemical findings, permits the conclusion that the involvement of the nervous system is localized in the mesodiencephalic region. Such activity is seen in persons subjected to high levels of exposure, particularly in the form of a pulsed field.

6. Possible explanations of the pathophysiology include direct penetration of the radiation into the midline structures and the thermal effect in the cisterna magna, which would explain the rare cases of arachnitis of the posterior fossae and the cerebellar phenomena. The rectangular branching of the blood vessels of the temporal and basal ganglia explains the slowing of the blood stream in these parts of the brain, accompanied by reduced oxygenation. It may be assumed that the subclinical paroxysmal activity is induced by alkalosis resulting from these disturbances.

7. The non-thermal effects and reversible neurotic manifestations may be attributed to the interruption of synaptic transmission and to changes in reflex activity under enzymatic influences.

8. In our considerations of the pathophysiology, we have concentrated on the fine regulatory mechanisms, which are disturbed before organic changes occur. The detection of these very early effects is important for preventive measures.

9. For a more precise evaluation of the technical parameters, further work will be necessary.

10. From our rather modest findings, it is nevertheless possible to deduce some preventive measures. Persons liable to paroxysmal activity of the central nervous system should be excluded from work involving exposure to non-ionizing radiation, and in certain cases persons with a pseudoneurasthenic syndrome or disturbances of motor systems may be unsuitable for work of this kind.

11. International and interdisciplinary collaborative studies are needed to develop such preventive measures in order to ensure that every worker will live and work under optimal conditions and will be enabled to use his knowledge and abilities to the full.

A STUDY OF THE HEALTH STATUS OF MICROWAVE WORKERS

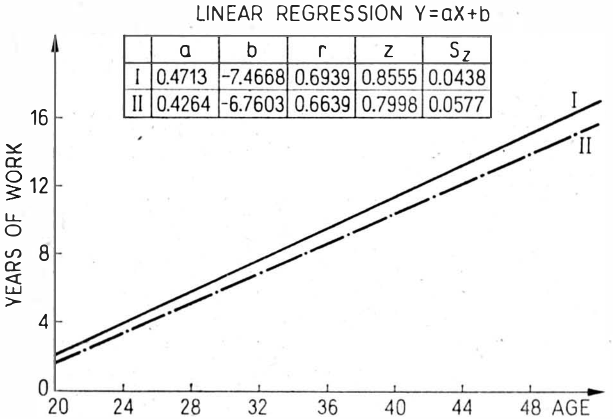
M. Siekierzyński

Institute for Postgraduate Study, Military Medical Academy, Warsaw, Poland

The study was undertaken of the health status of a group of 841 men aged from 20 to 45 years. All of them were occupationally exposed to irradiation with pulsed microwaves of various frequencies within the whole range used in radar operations.

They worked both in closed rooms and in the open, observing typical individual protective measures according to the regulations of work safety and hygiene existing in this country.

The field work performed was individually checked and the power density estimated. The population investigated was divided into 2 groups according to exposure levels. Figure 1 shows the correlation between age and duration of employment. The first group numbered 507 persons exposed during working hours at power densities above 2 W/m^2.



LINEAR REGRESSION Y=aX+b

	a	b	r	z	S_z
I	0.4713	-7.4668	0.6939	0.8555	0.0438
II	0.4264	-6.7603	0.6639	0.7998	0.0577

Fig. 1. Correlation between duration of occupational exposure (years of work) and age (years).

The second group included 334 persons exposed to a power density below 2 W/m^2. In both groups hygienic factors were comparable, i.e. the type and intensity of various stress factors, changes in circadian cycle, noise intensity, temperature and humidity of the rooms, etc.

All the persons in the study were examined at the same clinical center in stationary conditions from 1966 to 1972.

The program of clinical trials was typical for an internal medical clinic, including detailed ophthalmoscopic examination performed by means of a slit-lamp and a neurologic check-up, supplemented by psychologic tests and EEG recordings.

Both the ophthalmoscopic and neurologic examination were undertaken by the same specialists using the same classification of abnormalities. After the clinical observation period and possible treatment had been completed a decision was taken (according to the regulations existing in this country) as to the fitness of the individuals examined for further work in conditions of microwave exposure. In view of the difficulties of selection of an adequate control group for a population characterized by such specific work and exposure conditions, it was decided to compare the results obtained between the groups exposed to microwaves at two different power density levels as well as to analyse the relationship between the frequency of the characters investigated and the duration of employment and age.

Only selected data are discussed in this report, viz. those constituting the most frequent problems in determining the health status of the groups examined and their fitness for work. Thus, the causes of the unfitness for work in microwave exposure conditions, the frequency of what is called functional abnormalities and the lens translucency were analysed. In the analysis of causes of unfitness for work in both groups the following criteria were taken into account: eye changes, functional disturbances and finally all other causes taken together.

In the analysis of frequency of functional disturbances the patients were divided into subgroups with clinically apparent neurosis, neurosis with abnormal EEG patterns, gastrointestinal tract complaints of functional origin, and neurosis with abnormal ECG. The subgroup with abnormal EEG tracings included persons with various neurotic disturbances and distinct pathological EEG recordings as well as flat EEG recordings, i.e. with the frequency of α-waves decreased to 20 per cent and the amplitude of these waves lowered to 20 mV. Abnormalities in ECG recordings concerned mostly a partial block of the right His bundle. None of the patients in this group had organic heart muscle lesions. Lens translucency was determined according to the scale proposed by Dr. Żydecki (this volume).

The frequencies of the characters examined (mean percentages) in the first and second group and the correlation of their occurrence with the duration of employment and age were analysed statistically.

Here Student's t test was used and the standard deviations were compared by the F test of Fisher (2).

Correlation analysis was carried out using the mean square test (for multi-area tables), while the determination of the reciprocal coupling was made using the Čupurov coefficient. The statistical significance level has been set as 0.05.

In subgroups in which the independency test indicated a statistically significant correlation between characters investigated, this was analysed by drawing regression lines and by determination of the regression coefficient. The significance of the correlation coefficient was verified according to Fisher's transformation (2).

Table 1

The structure of groups I and II according to duration of employment and age

Group	Duration of employment			Total	Age			
	1—5	6—10	10		20—25	26—30	31—35	36—45
I	193	207	107	507	125	158	109	115
II	134	114	86	334	73	67	65	129

Table 2

Comparison of mean percentage values of corresponding data of groups I and II as divided according to the age

			x_1	S_1	x_2	S_2	ItI	F	
Fitness for work									$n_1\ n_2 = 13$
		Able	47.9	12.1	47.3	16.0	0.109	1.741	$K = 24$
	Cause of unfitness	Ophthalmologic	8.2	4.3	10.1	5.2	1.006	1.475	$f_1\ f_2 = 12$
		Functional	29.3	7.7	28.7	13.1	0.137	2.849	Verified:
		Other	14.6	8.4	13.9	5.5	0.263	2.327	ItI to $t_{0.05;\,24} = 2.064$ F to $F_{0.05;\,12;\,12} = 2.690$
Incidence of functional disorders	None		37.2	11.7	34.3	11.8	0.605	1.015	$n_1\ n_2 = 12$
	Neurosis		34.2	9.6	31.8	6.0	0.738	2.549	$K = 22$
	Gastrointestinal tract		19.7	6.5	23.5	8.5	1.236	1.721	$f_1\ f_2 = 11$ Verified:
	Abnormal ECG		8.8	3.4	10.4	3.3	1.154	1.018	ItI to $t_{0.05;\,22} = 2.074$ F to $F_{0.05;\,11;\,11} = 2.850$
Lens translucency	1°		28.1	11.7	22.0	15.3	1.141	1.714	$n_1\ n_2 = 13$
	2°		23.4	13.5	58.8	15.5	0.940	1.309	$K = 24$
	3° and higher		18.3	14.8	19.1	8.9	0.157	2.766	$f_1\ f_2 = 12$ Verified: ItI to $t_{0.05;\,24} = 2.064$ F to $F_{0.05;\,12;\,12} = 2.690$

Explanations:
$x_1\ x_2$ — mean values
$S_1\ S_2$ — standard deviations
$n_1\ n_2$ — number of results
ItI — module of Student's t-test
K — degrees of freedom
F = F — number of Fisher's test
$f_1\ f_2$ — degrees of freedom

T a b l e 3

Comparison of mean percentage values of corresponding data of group I and II as divided according to the duration of employment

			x_1	S_1	x_2	S_2	I t I	F	
Fitness for work	Causes of unfitness	Able	51.5	18.7	43.7	15.1	1.332	1.523	n_1 n_2 = 17 K = 32 f_1 f_2 = 16 Verified: I t I to $t_{0.05;\,32}$ - 2.042 F to $F_{0.05;\,16;\,16}$ - 2.350
		Ophthalmologic	8.0	5.2	10.3	6.2	1.144	1.427	
		Functional	28.1	10.5	30.4	8.8	0.684	1.429	
		Other	12.7	7.4	15.2	8.1	0.931	1.208	
The frequency of functional disorders		None	37.1	17.8	30.4	9.5	1.635	3.546	n_1 n_2 = 17 K = 32 f_1 f_2 = 16 Verified: I t I to $t_{0.05;\,32}$ - 2.042 F to $F_{0.05;\,16;\,16}$ - 2.350
		Neurosis	35.1	9.7	34.2	8.4	0.288	1.334	
		Gastrointestinal tract	21.6	9.3	22.9	8.4	0.429	1.222	
		Abnormal ECG	8.2	4.5	11.4	5.5	1.272	1.478	
Lens translucency		1°	27.5	13.1	23.6	12.5	0.885	1.103	n_1 n_2 = 17 K = 32 f_1 f_2 = 16 Verified: I t I to $t_{0.05;\,32}$ - 2.042 F to $F_{0.05;\,16;\,16}$ - 2.350
		2°	53.3	9.8	56.8	13.5	0.860	1.872	
		3° and higher	22.4	18.2	19.4	8.3	0.610	4.754	

Explanations:

x_1 x_2	— mean values	ItI	— module of Student's t-test
S_1 S_2	— standard deviations	K	— degrees of freedom
n_1 n_2	— number of results	F — F	— number of Fisher's test
f_1 f_2	— degrees of freedom		

RESULTS

Results of the statistical analysis are presented in successive tables. Table 2 shows a comparison between groups I and II with respect to the mean values of the characters analysed, according to age. The same comparison as related to the duration of employment is presented in Table 3. No statistically significant differences were found among these groups. The calculated I t I value was lower than that given in the statistical tables. The results of the correlation analysis between characters investigated and age separately for each group are shown in the next tables.

Table 4

Analysis of the relationship between fitness for work, duration of employment and age in group I

Fitness ability for work		Duration of employment			Total	Age			
		1—5	6—10	10		20—25	26—30	31—35	36—45
Fit		107	102	59	268	69	80	53	66
Causes of unfitness	Ophthalmologic	16	20	13	49	14	11	12	12
	Functional	42	53	15	110	25	41	27	17
	Other	28	32	20	80	17	26	17	20

$p = 0.31506$
$\chi^2 = 7.06300$
$K = 6$
$\varphi^2 = 0.01393$
$K = 0.00569$

$p = 0.53686$
$\chi^2 = 7.97312$
$K = 9$
$\varphi^2 = 0.01573$
$K = 0.00524$

Table 5

Analysis of the relationship between fitness for work, duration of employment and age in group II

Fitness for work		Duration of employment			Total	Age			
		1—5	6—10	10		20—25	26—30	31—35	36—45
Fit		74	51	42	167	52	30	35	50
Causes of unfitness	Ophthalmologic	14	17	9	40	5	7	10	18
	Functional	34	23	23	80	10	19	10	41
	Other	12	23	12	47	6	11	10	20

$p = 0.16180$
$\chi^2 = 9.21574$
$K = 6$
$\varphi^2 = 0.02759$
$K = 0.01126$

$p = 0.00353$
$\chi^2 = 24.35290$
$K = 9$
$\varphi^2 = 0.073345$
$K = 0.02448$

Each of the multi-area tables includes the results of statistical analysis, i.e. the: probability p distribution, degree of freedom k, correlation coefficient and Čupurov coefficient K. The Table 4 represent the results of the analysis of the dependence between the ability to work and the duration of employment and the age of the population of group I, while in Table 5 the same analysis is shown for group II.

No statistically significant correlation was found between the causes of the unfitness for work and the duration of employment in the two groups. A significant probability factor in group II divided according to age is characterized by a very low Čupurov coefficient of reciprocal dependence. Table 6 shows the results of the analysis of correlation between the occurrence of functional disorders and the duration of employment and age of the investigated persons of group I, while the same analysis for group II is given in the Table 7.

Table 6

Analysis of the relationship between the incidence of functional disorders, duration of employment and age in group I

Functional Disorders	Duration of employment			Total	Age			
	1—5	6—10	10		20—25	26—30	31—35	36—40
None	83	68	39	190	63	58	26	43
Neurosis	64	78	38	180	38	64	49	29
Gastrointestinal	26	38	23	87	10	23	24	30
Abnormal ECG	20	23	7	50	14	13	10	13

$p = 0.14777$
$\chi^2 = 12.07780$
$K_2 = 8$
$\varphi^2 = 0.02382$
$K = 0.00842$

$p = 0.00002$
$\chi^2 = 43.26527$
$K_2 = 12$
$\varphi^2 = 0.08534$
$K = 0.02463$

Table 7

Analysis of the relationship between the incidence of functional disorders, duration of employment and age in group II

Functional Disorders	Duration of employment			Total	Age			
	1—5	6—10	10		20—25	26—30	31—35	36—45
None	50	31	27	107	32	22	21	33
Neurosis	40	41	35	116	23	25	20	48
Gastrointestinal	29	33	16	78	10	14	19	35
Abnormal ECG	15	9	8	32	8	6	5	13

$p_2 = 0.26254$
$\chi^2 = 10.03560$
$K_2 = 8$
$\varphi^2 = 0.03005$
$K = 0.01062$

$p_2 = 0.14367$
$\chi^2 = 17.16013$
$K_2 = 12$
$\varphi^2 = 0.05138$
$K = 0.01483$

The occurrence of statistically significant differences was found only for group I, in relation to age. No correlation of the occurrence of these disorders with the duration of employment could be demonstrated. An additional analysis of dependence of the occurrence of functional disorders in relation to age does not indicate any linear relationship.

Table 8 shows the analysis of the correlation between the lens translucency, duration of employment and age in group I, while Table 9 represent a similar analysis for group II.

Table 8

Analysis of the relationship between lens translucency duration of employment and age in group I

Lens translucency	Duration of employment			Total	Age			
	1—5	6—10	10		20—25	26—30	31—35	36—45
1°	71	24	16	141	55	45	26	15
2°	95	108	67	270	54	89	60	67
3° and higher	27	45	24	96	16	24	23	33

$p_2 = 0.00094$
$\chi^2 = 18.61215$
$K_2 = 4$
$\varphi^2 = 0.03671$
$K = 0.01836$

$p_2 = 0.00001$
$\chi^2 = 34.40868$
$K_2 = 6$
$\varphi^2 = 0.06787$
$K = 0.02771$

Table 9

Analysis of the relationship between lens translucency, duration of employment and age in group II

Lens translucency	Duration of employment			Total	Age			
	1—5	6—10	10		20—25	26—30	31—35	36—45
1°	50	30	19	99	32	24	18	25
2°	65	61	49	175	32	40	40	63
3° and higher	19	23	18	60	9	3	7	41

$p_2 = 0.12097$
$\chi^2 = 7.29769$
$K = 4$
$\varphi^2 = 0.02185$
$K = 0.01092$

$p_2 = 0.00000$
$\chi^2 = 37.20359$
$K = 6$
$\varphi^2 = 0.11139$
$K = 0.04547$

Statistically significant correlation exists in both groups between lens translucency and age, but between lens translucency and duration of employment in group I only.

A regression analysis of the degree of lens translucency as a function of age and of the duration of employment was made.

Additional regression analysis was made as a function of age and duration of employment. The results are shown in Table 2. A linear regression slope was obtained, the correlation coefficient indicating a highly significant correlation between the age and the duration of employment.

DISCUSSION

The occupationally exposed group of persons who formed the subject of this study should be considered as highly preselected.

Approximately one half of the examined persons consists of workers in institutions where high exposures to irradiation occur and considering this in the light of the field measurements made, it may be said that the above mentioned data are representative of the most exposed group in this country. At the initial stage of this analysis several trials were performed in dividing investigated populations into a greater number of subgroups according to age, duration of employment and other characteristics. If both groups, however, had been divided into subgroups the number of individual observations in each particular group would not have reached the minimum required for valid statistical analysis.

Besides exposure to microwaves several hygienic factors were analysed, i.e. such as could exert a negative influence on the health status of the investigated population. In practice a control group for a population with such specific working conditions does not exist.

In view of this no traditional comparison of incidence of deviations from normal values inside each investigated group and no comparison with what is called "standard man" was made. Taking the above-mentioned complex conditions of irradiation into, account, such calculated deviations could not be related to the effects of microwave exposure. The present paper describes only a part of the analysis performed, viz.: the causes of unfitness for work, the determination of lens translucency and the incidence of several neurotic disturbances — that means the problems considered as related to the influence of the microwave irradiation on the human organism, especially stressed in testing the fitness for work in conditions of exposure to microwaves. The analysis of the data indicate an absence of differences between the groups exposed in various degrees to microwaves and an absence of correlation of incidence of the investigated characteristics with the duration of employment, in contradistinction to the obviously existing correlation between certain characters and age.

For example a decreasing frequency of 1° in lens translucency proportional to age has been observed. This may indicate that microwave irradiation by itself does not influence the incidence or quality of the characters analysed in an exposed population. The final conclusion is: the analysis within the groups, as well as between groups of persons occupationally exposed to various power densities of microwave radiation does not indicate a correlation between the degree of exposure or duration of employment in conditions of exposure and the incidence of the analysed health disturbances and the degree of lens translucency.

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BLOOD PROTEINS IN PERSONNEL OF TELEVISION AND RADIO TRANSMITTING STATIONS

J. Pazderová, J. Picková and V. Bryndová

University Department of Occupational Diseases, Faculty of General Medicine, Charles University, Prague; Research Institute of Telecommunication, Prague, Czechoslovakia

In an earlier paper the influence of working conditions on the state of health of the staff of the TV and radio transmitting stations in Czechoslovakia was studied (4, 5). 140 persons were carefully examined (Tab. 1) during hospitalization, which represented about $^2/_3$ of all employees with an exposure time of more than 5 years. The results were compared with those in control groups and statistically evaluated.

Table 1

Review of clinical and laboratory examinations

Laboratory examinations	**Clinical examinations**
Analysis of urine	Physical
Blood count	Neurologic
BSR	Psychologic
BMR	Psychiatric
Liver tests + Transaminase	Ophthalmologic
Proteinalysis	
Blood sugar curve	
Cholinesterase activity	
X-ray of chest	
ECG	
EEG	

No signs of damage due to electromagnetic radiation nor any changes in health status were ascertained with the exception of modifications in the blood protein ratio. The mean percentage of gamma-globulin was increased in the personnel of radio transmitting stations (20.2—21.0% in comparison to 18.3% in the control group), as well as the total blood protein level in the staff of the TV transmitters (7.6 g% : 6.9 g% in the control group). Small differences in the alpha$_1$-globulin were also found in certain groups. Though all individual and average values were within physiologic limits, the statistical differences in the mean values of the exposed and control groups were confirmed by means of the F-test and the Duncan test at a 1% or 5% confidence level.

We did not feel sure whether these alterations were caused by electromagnetic fields or if they could have been due to other factors. The exposed persons came from all parts of Czechoslovakia, especially from the countryside and mountainous regions, whereas the members of the control group lived in the capital and differed in their living standards, habits and nutrition. Another factor which caused doubt was that the protein analyses were made in a routine biochemical laboratory where the possibility of the inaccuracies that frequently occur in this type of work could not be excluded.

In order to eliminate the above-mentioned sources of error and to elucidate the possible influence of electromagnetic radiation on the blood proteins, we repeated the investigation on all TV and radio transmitter technicians in Bohemia who have been working for at least 5 years in their profession. This paper deals with the final conclusions drawn from the investigations on TV technicians and the preliminary results of the investigations carried out on radio technicians.

The characteristics of the working and environmental conditions are given in the following tables.

The transmitters broadcast in the usual TV, SW and MW frequencies (Tab. 2).

Table 2

Frequencies of electromagnetic radiation

TV	60--300 MHz
SW	3--30 MHz
MW	640—1500 kHz

The intensity of the electromagnetic fields in the TV stations (Fig. 1.) was estimated by means of a Režný apparatus, which measures the integral intensity of electromagnetic fields. In radiostations the universal wide-zone voltmeter B 388 A was used. The error of the former method reaches up to ± 30%, and of the latter up to ± 100%. Only the electric, but not the magnetic component of the field was measured. The Czechoslovak maximum permissible level corresponds to 10 V/m. Higher values were found only rarely in one station. The number of persons investigated in every TV station is

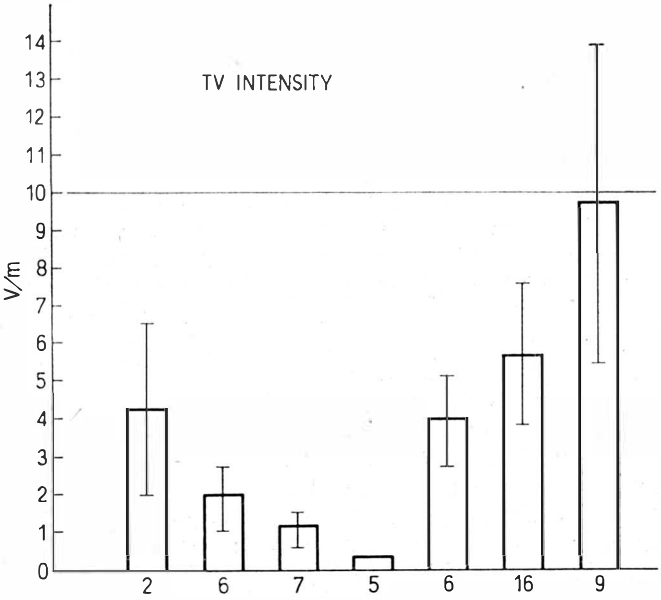

Fig. 1. Intensity of electromagnetic fields in TV stations.

given below the vertical columns, which represent the mean intensity at the stations with their standard deviations.

The values of irradiation for one working day equal the sum of the intensity of the electromagnetic field (V/m) and the time of exposure (number of hours in one working day) (Fig. 2).

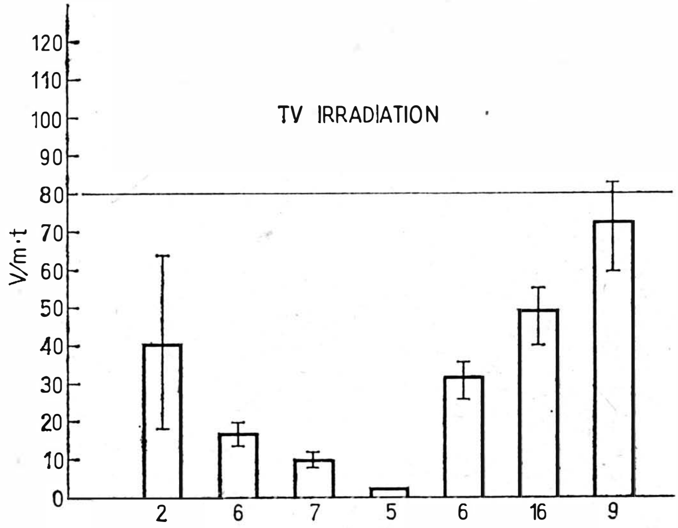

Fig. 2. Values of irradiation in TV stations.

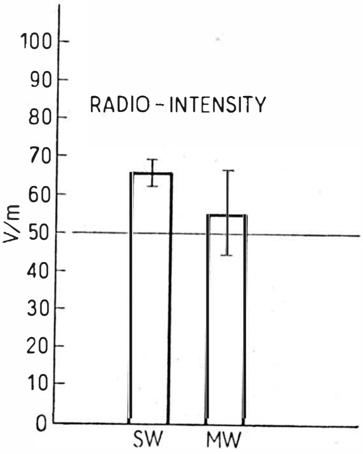

Fig. **3**

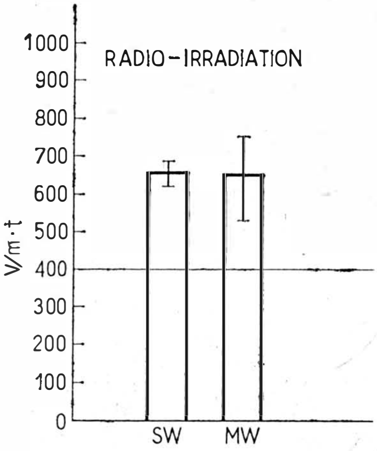

Fig. **4**

Fig. 3. Intensity of electromagnetic fields in radio transmitters.
Fig. 4. Values of irradiation in radio transmitters.

The maximum permissible value for these frequencies in Czechoslovakia is 80. Practically all measurements were within these limits.

The intensities of electromagnetic fields in radio transmitting stations (Fig. 3) were higher than the permissible maximum of 50 V/m in the majority of measurements. The same applies to the irradiation values for the radiowaves (Fig. 4) (maximum permissible value 400).

The work is done in light, well-equipped rooms with agreeable microclimate conditions. The noise level varied in TV stations within the range of the class of noise N 65 — 81 and in radio transmitters 65 — 71.

The employees of the transmitters worked a 40.5 hour week in irregular shifts.

The characteristics of the persons examined are given in Table 3.

Table 3

Characteristics of persons examined

	Controls	TV	SW	MW
No. of workers			58	
	59	51	19	39
Mean age	35.4	35.2	39.3	41.3
± s.d.	9.0	6.2	6.3	9.7
Mean years of exposure		10.4	16.8	16.8
± s.d.	—	3.5	7.8	4.9

The mean age of the control group is approximately the same as that of the exposed persons. The control group was chosen from the same regions as the exposed persons, and from the same social standard and living conditions. The only difference is that the exposed technicians worked in irregular shifts, while more than half of the people in the control group only worked morning shifts, but we have not found any data in the literature describing any influence of irregular shifts on the blood proteins.

The persons were examined and blood was taken during their working shifts in the transmitting stations. Each blood sample was examined twice in our laboratory. Total serum proteins were calculated from the nitrogen balance estimated by the colorimetric Nessler method (3). Fractions of proteins were separated by means of paper electrophoresis (6). Differences in the results of the two examinations of one person did not exceed 1 %. For statistical evaluation the F-test and the Duncan test were used.

RESULTS

As our previous work did not reveal any pathologic changes attributable to the influence of electromagnetic radiation, the physical examination aimed mainly at excluding patients with the kinds of disease which are known to influence the blood chemistry.

The levels of blood proteins and their fractions were within physiologic limits, both mean values and individual ones, but statistically significant differences were found between the mean values for the control and exposed groups.

Total protein level (Fig. 5) was higher in people operating medium wave transmitters. One asterisk indicates the 5% and two asterisks the 1% level of confidence. The albuminoglobulin quotient (Fig. 6) decreased in radiotechnicians, which was due to the drop in albumin (Fig. 7) and increase in alpha$_1$ (Fig. 8) and beta globulin (Fig. 9 Alpha-$_2$

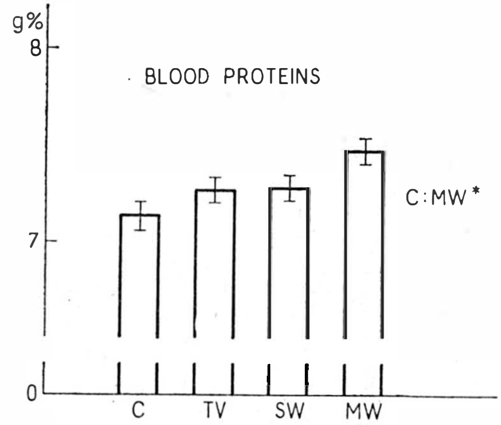

Fig. 5. Total blood protein level.

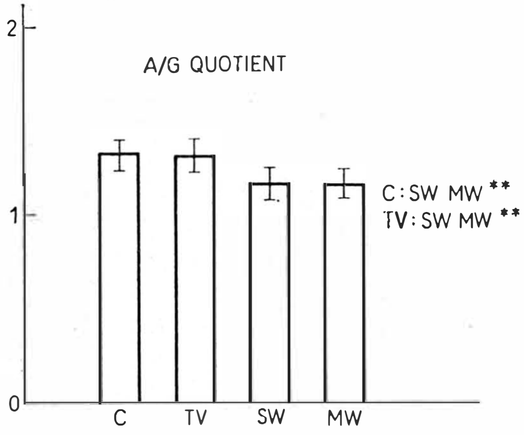

Fig. 6. Albumino-globulin quotient.

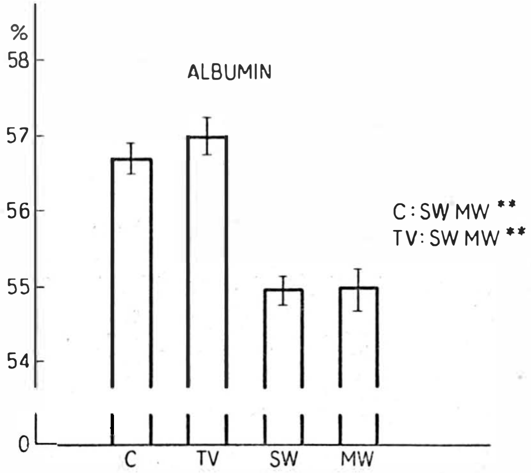

Fig. 7. Level of albumin.

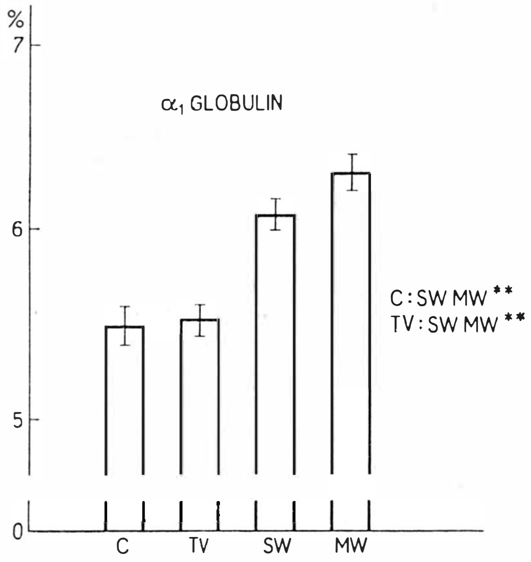

Fig. 8. Level of alpha$_1$ globulin.

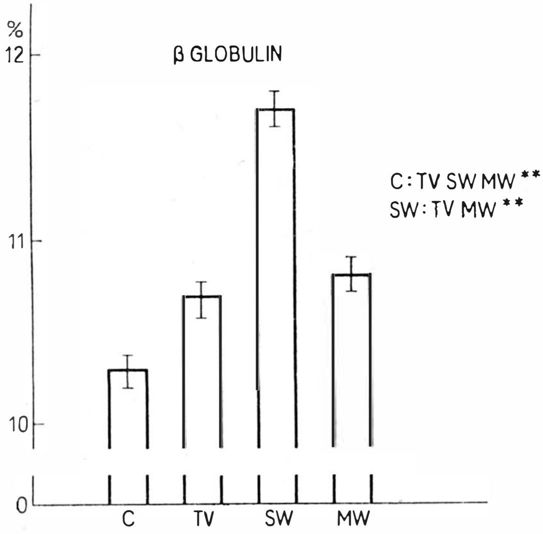

Fig. 9. Level of beta globulin.

globulin did not show any significant changes (Fig. 10). These alterations — with the exception of the increase in beta globulin — were not present in TV technicians, the most striking change being the decrease in gamma-globulin (Fig. 11).

DISCUSSION

This investigation has been carried out in such a way that sources of error in particular in the selection of the control group and laboratory procedures were dimin-

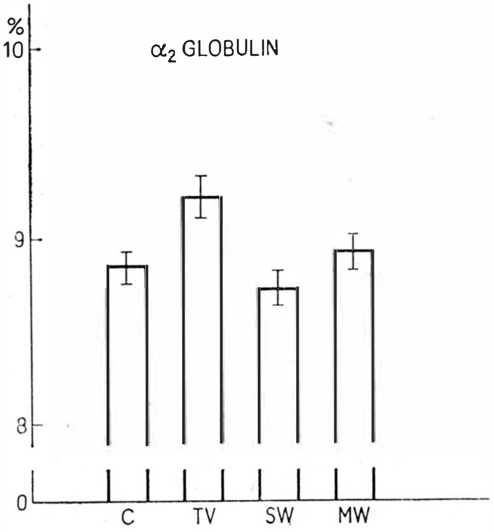

Fig. 10. Level of alpha$_2$ globulin.

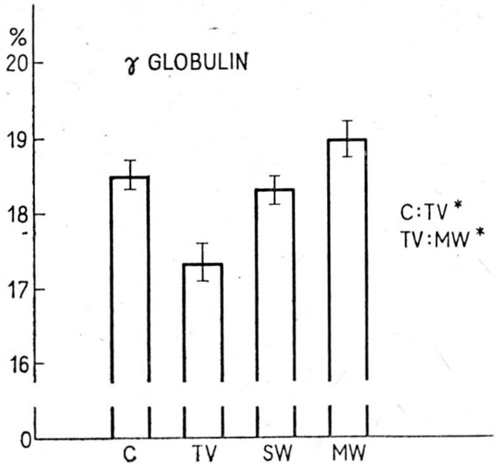

Fig. 11. Level of gamma globulin.

ished. Our previous findings confirmed the data from the literature (1, 2, 7, 8, 9) on the existence of blood protein changes in persons and experimental animals exposed to electromagnetic radiation. To our great surprise, the character of the changes diverged from those so far described, as we did not find any elevation of gamma-globulin, which is considered to be typical. We are unable to explain this difference, unless we attribute it to the fact that, contrary to our previous investigation, blood was taken directly at the transmitting stations immediately after exposure to electromagnetic fields. This explanation still remains open to discussion. The more pronounced changes in radio technicians might be ascribed to the higher and longer exposures in comparison with TV technicians.

It must be emphasized that no pathologic findings have been revealed either in clinical or in laboratory examinations. The values of blood proteins were all within normal limits and only a difference in mean values could be proved statistically between the exposed and control groups. These differences could be considered as a general response of the organism to the stress of electromagnetic radiation, like similar reactions to other factors, chemical or biologic. This response, however, is not to be considered as a pathologic state.

We intend to continue studies to further elucidate the processes involved.

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THE BIOLOGIC ACTION AND HYGIENIC SIGNIFICANCE OF ELECTROMAGNETIC FIELDS OF SUPERHIGH AND ULTRAHIGH FREQUENCIES IN DENSELY POPULATED AREAS

J. D. Dumanskij and M. G. Šandala

A. N. Marzeev Kiev Scientific Research Institute of General and Public Hygiene, USSR

With the powerful development of television, radar, radioastronomy and radiometeorology, hygienists are faced with a number of tasks, one of which is the assessment of energy of ultrahigh (UHF) and superhigh (SHF) ranges in densely inhabited areas. Until recently these ranges of radiofrequencies were investigated by hygienists only from the point of view of industrial hygiene and occupational diseases, while the problems of the biologic action and hygienic significance of UHF and SHF ranges, in relation to public hygiene, remained insufficiently elucidated. Taking this into account, we performed special investigations both on the distribution of electromagnetic energy in the UHF and SHF ranges under modern urban conditions and on the biologic effects of this energy.

Results of these investigations showed that at sites where television transmitters, TV links and radar stations are placed, the intensity of electromagnetic energy is much higher than that of the earth's background and covers a wide range, depending on the capacity of the emitters and the distance from radiating devices (antenna). Electromagnetic energy of various intensities penetrates living, administrative and other buildings located in the vicinity of the sources of radiation.

In order to assess the biologic action of the defined intensities of electromagnetic energy, as well as the hygienic importance of such radiation in densely populated areas, experimental studies on animals were conducted. Investigations were performed in shortened wave guides within the ultrahigh frequency range (wavelength 6 m) at the following power densities: 10, 2.4, 1.9, 0.06, 0.01 and 0.0006 $\mu W/cm^2$. Within the range of superhigh frequencies, irradiation was carried out at a distance which corresponded to the following power densities: 10, 5, 1 and 0.5$\mu W/cm^2$ (continuous generation, 12 cm wavelength) and 10, 5, and 1 $\mu W/cm^2$ (pulsed generation, 3 cm wavelength, pulse duration $\tau = 1$ μsec and 1000 and 20 pulses per second).

In addition, using the pulsed regime of irradiation, the movements of the radar antenna were imitated with a beam angle of 2° and a rotation frequency of 10 revolutions per minute.

The computed intensities were close to those encountered in areas adjacent to television transmitters, links and radar systems.

The intensity of electromagnetic energy during experiments was controlled with IEMP-1 and PTSH-5A instruments for the UHF range and PO-1 ("Medik") for the SHF range.

Investigations of biologic effects for the UHF range were conducted on 128 white rats and 28 rabbits, and for the SHF range on 100 white rats and 32 rabbits. The animals were irradiated daily for 10—12 h with electromagnetic energy in the UHF range and for 8 h in the SHF range. For each range and each intensity, the duration of the experiment amounted to 180 days (120 days of irradiation and 60 days of follow-up).

The results showed that the action of the electromagnetic field both in the UHF and SHF ranges during the first 10—12 days of irradiation resulted in some changes in the general status of the organism. Within this period the animals were somewhat excited and reacted to switching-on of the electromagnetic field.

These findings substantiated the notion that, as a result of the action of the electromagnetic energy, certain changes in the central nervous system were elicited. In order to define the changes more closely, investigations of the conditioned reflex activity of the animals were performed.

These experiments showed that, under the action of UHF and SHF fields, certain periodic changes appeared in the conditioned reflex activity of the animals. On the whole, the latent period was longer, reflex reactions to positive stimuli weakened, and the number of those missing increased. All this was evidently connected with the development of consequent inhibition related to impairment of nervous reactivity, and leading to pathologic stagnation and inertia. The intensities which produced statistically significant changes were 1.9—10 μW/cm^2 and 5—20μW/cm^2 in the UHF and SHF ranges, respectively.

These data were supplemented by electroencephalographic studies conducted on rabbits. The dynamics of changes in the central nervous system were assessed, as reflected in bioelectric activity of the brain cortex. The results showed that in the investigated rabbits the action of electromagnetic energy elicited some disturbances in relations between the potential frequency groups of the cortex (Tab. 1). At the beginning (2—14 days), activition of the biocurrents in the brain was observed, testifying

Table 1

Changes in biocurrents in the brain cortex of rabbits under the influence of electromagnetic energy of UHF range

Groups of animals and field intensity	Rhythms of biocurrents	Periods of examination				
		Before irradiation	2 days later	10 days later	30 days later	60 days later
Group I 10 μW/cm^2	Slow	26.0 ± 1.8	11.0 ± 1.8	6.0 ± 1.6	17.0 ± 2.9	58.2 ± 5.1
	intermediate	50.1 ± 1.7	34.0 ± 4.1	24.5 ± 2.7	54.2 ± 3.3	27.2 ± 1.9
	fast	23.1 ± 0.6	55.0 ± 5.8	72.0 ± 1.7	29.8 ± 0.7	11.6 ± 3.1
Group II 1.9 μW/cm^2	Slow	19.0 ± 2.1	11.5 ± 1.0	16.0 ± 1.7	12.8 ± 2.2	52.0 ± 2.7
	intermediate	66.4 ± 3.2	72.0 ± 3.3	46.0 ± 8.5	65.0 ± 3.9	38.6 ± 4.8
	fast	14.2 ± 1.6	16.5 ± 2.5	44.0 ± 9.7	22.2 ± 4.6	9.2 ± 2.3
Group III 0.01 μW/cm^2	Slow	18.7 ± 1.4	19.0 ± 1.6	17.5 ± 1.7	14.0 ± 1.2	22.5 ± 1.4
	intermediate	70.2 ± 0.9	70.0 ± 2.2	68.5 ± 2.9	69.5 ± 2.4	65.0 ± 2.9
	fast	10.5 ± 0.9	11.0 ± 1.7	14.0 ± 1.9	11.0 ± 1.7	11.0 ± 2.2
Controls	Slow	17.2 ± 1.4	17.2 ± 1.4	14.8 ± 0.7	14.2 ± 0.8	16.0 ± 0.4
	intermediate	65.7 ± 2.4	67.7 ± 2.4	68.2 ± 1.4	70.7 ± 1.8	67.8 ± 0.4
	fast	16.6 ± 1.2	16.6 ± 1.2	17.0 ± 2.0	15.6 ± 1.9	16.2 ± 0.7

to some increase in the excitation process. With increasing duration of exposure an initial stage of inhibition developed, characterized by synchronization of the cortical rhythms. Thus, upon prolonged irradiation, the strength of the process of inhibition within the brain hemisphere cortex was appreciably increased, as evidenced by the appearance of slow rhythms in the electroencephalograms. The observed changes in bioelectric activity of the brain cortex of rabbits confirmed previously reported results of studies on conditioned reflex activity of animals and showed that electromagnetic energy in the UHF range and 0.06—10 μW/cm² intensity, as well in the as SHF range and 5—20 μW/cm² intensity, was indeed active biologically according to the results of statistical analysis.

Bearing in mind that electromagnetic fields of radiowaves act predominantly on the central nervous system, our biochemical studies concentrated on those indicators which directly or indirectly characterized the functional activity of the nervous system. Such tests in our investigations included cholinesterase activity and sulphydryl (SH) groups in the blood.

These experimental investigations showed that electromagnetic fields in the UHF and SHF ranges appreciably lowered blood cholinesterase activity and quantity of SH groups (Tab. 2 and 3). It could be noted that with increasing duration of exposure to the field, inactivation of SH groups in the blood also increased. It could therefore be assumed that a lowered activity of both cholinesterase and SH groups in the blood, as induced by the action of UHF and SHF electromagnetic energy, resulted in impairment of the biochemical mechanisms which ensure the normal course of nervous processes in the animal organism. Such was the likely explanation of the

Table 2

Changes in certain indicators of metabolic processes in rats exposed to UHF electromagnetic energy in chronic experiments

Indicator	Group I, 10 μW/cm²				Group II, 1.9 μW/cm²				Group III, 0.01 μW/cm²			
	Before irradiation	30 days later	90 days later	120 days later	Before irradiation	30 days later	90 days later	120 days later	Before irradiation	30 days later	90 days later	120 days later
Blood cholinesterase activity, ΔA/min	154	121	84	98	154	152	108	101	156	152	151	173
± S.D.		3.8	7.2	5.0		0.3	6.0	6.9		0.4	0.5	1.9
Blood SH groups, μmol/100 ml	1697	1750	1410	1190	1500	1340	1030	857	1702	1537	1587	1550
± S.D.		0.8	4.0	6.6		3.1	7.3	10.8		1.8	0.8	0.5
17-ketosteroids, in urine, mg/24 h	0.019	0.032	0.055	0.060	0.018	0.024	0.040	0.047	0.021	0.018	0.022	0.023
± S.D.		8.6	19.4	16.4		2.7	8.4	10.4		0.7	1.2	0.4

Table 3

Changes in certain indicators of metabolic processes in rats exposed continuously to SHF electromagnetic energy in chronic experiments

Indicator	Group I, 10 μW/cm^2				Group II, 5 μW/cm^2				Controls			
	Before irradiation	30 days later	90 days later	120 days later	Before irradiation	30 days later	90 days later	120 days later	Before irradiation	30 days later	90 days later	120 days later
Blood cholinesterase activity, ΔA/min	123	142	110	104	125	134	110	110	123	122	122	147
p		<0.05	<0.05	<0.05		<0.05	<0.05	<0.05				
Blood SH groups, μmol/100 ml	1411	1694	1320	1340	1427	1640	1340	1350	1461	1461	1527	1533
±S.D.		5.7	2.5	2.2		3.6	2.8	2.9		0	1.0	1.1
17-ketosteroids in urine, mg/24 h	0.0225	0.0375	0.0368	0.0343	0.0230	0.0380	0.0375	0.0420	0.0230	0.0256	0.0243	0.0213
p		<0.05	<0.05	<0.05		<0.05	<0.05	<0.05				
RNA in the liver	—	—	—	70.2	—	—	—	71.4	—	—	—	89.3
±S.D.	—	—	—	4.9	—	—	—	3.6				
DNA in the liver	—	—	—	51.5	—	—	—	51.0	—	—	—	70.7
±S.D.	—	—	—	5.0	—	—	—	5.0				

changes which we found in conditioned reflex and bioelectric activities of the brain cortex of irradiated animals.

It is well known that steroid adrenal hormones, weight of the suprarenal glands and their ascorbic acid contents are all important biochemical parameters of metabolic processes of the human and animal organism. These parameters characterize not only general metabolic processes of the organism, but also reflect certain relations between biochemical reactions and the functional status of the nervous system, and are therefore of particular interest.

Our results showed that prolonged action of electromagnetic fields of UHF and SHF frequencies resulted in increased weight of the adrenals, a reduction in their ascorbic acid content and increased secretion of 17-ketosteroids in the urine of experimental animals. The above changes could probably be explained by an increased functional activity of the hypophysis-adrenal cortex system. It is widely accepted that activation of the cortical function points to an influence of unfavourable conditions, so-called stress stimuli, acting upon the whole organism. In this case we considered electromagnetic fields in the UHF and SHF ranges to be such unfavourable stimuli. The lesions occured in animals irradiated at power densities of 0.06 to 10 and 5 to 20 μW/cm² with UHF and SHF electromagnetic fields, respectively.

While investigating the biologic influence of electromagnetic fields in the SHF range, we tried to define the action of this factor upon the endocrine system and took as an example the thyroid gland. In order to asses the functional status of the thyroid, use was made of the radioactive iodine indicator method (uptake of radioactive iodine by the thyroid gland) and the method employing ^{131}I-thyroxine. These investigations showed that under the influence of SHF fields of 10, 5 and 1 μW/cm² power density, the ability of the thyroid gland to concentrate radioactive iodine was increased: the maximum uptake amounted to 48.0 ± 1.88 at 10 μW/cm², 51.2 ± 4.03 at 5 μW/cm², and 51.1 ± 6.0 at 1 μW/cm², as compared with 28.3 ± 3.38 in control animals. This testified to the fact that SHF energy induced intensification of thyroid function. Taking into account that the thyroid gland has a regulatory influence on a number of functions of the organism, one could imagine that an increase in its activity induced a number of undesirable changes in the organism as a whole.

The above investigations were accompanied by studies on the morphologic composition of the blood. It was found that electromagnetic energy in the UHF and SHF ranges caused an insignificant decrease in the number of leukocytes, eosinophils and reticulocytes; some tendency to lowered erythrocyte and hemoglobin values was also observed.

Bearing in mind that electromagnetic fields influence general metabolic processes, we performed investigations on the effects of this factor on nucleic acid metabolism. Results of these investigations showed that the factor under study induced a statistically significant increase in the RNA and DNA contents of the spleen and liver of the animals (see Tab. 2). It is difficult at present to explain these findings. To solve this problem, special investigations will be needed.

In addition, we studied the influence of electromagnetic energy in the UHF range upon carbohydrate-phosphorus metabolism. These investigations showed that a prolonged exposure to a field of 0.06—10 μW/cm² intensity resulted in disturbances of glycogen metabolism, i.e. a reduction in the glycogen content in the liver due to increased phosphorylase activity accompanied by simultaneous accumulation of lactic acid. At the same time a marked influence of UHF fields on oxidative coupling and phosphorylation processes in rat liver mitochondria was detected. Long-term irradiation led to a fall of phosphorylation and oxidation functions of hepatic mitochondria.

The biologic experiments were complemented by histomorphologic studies which showed that the lesions which appeared under the influence of electromagnetic energy in the UHF and SHF ranges took the form of dystrophic changes in the brain, liver, spleen and testes, along with impairment of blood circulation. The severity of these changes depended on the intensity of the electromagnetic field. More pronounced changes were found in the organs of animals exposed to relatively high intensities.

Analysing the results of the above experimental investigations, it should be noted that prolonged action of electromagnetic energy of low intensities in the UHF and SHF ranges resulted in appreciable changes in the general status of the organism, conditioned reflex activity, bioelectric activity of the brain cortex, a number of biochemical parameters, blood composition and morphologic structures of the tissues and organs of the animals under study. The biologically active intensities of electromagnetic fields were 10—0.06 and 20—5 μW/cm² for UHF and SHF ranges, respectively.

SELECTED CASES OF MICROWAVE CATARACT IN MAN ASSOCIATED WITH CONCOMITANT ANNOTATED PATHOLOGIES

M. M. Zaret

Zaret Foundation, Scarsdale, New York, U. S. A.

INTRODUCTION

In man, microwave radiation can cause cataracts via several different mechanisms. Only rarely is exposure relatable to or associated with clinically recognizable thermal injury. Ordinarily, there are no signs or symptoms suggesting thermic insult. Instead, the irradiations usually occur without the subject displaying any sense of awareness.

Where microwaves serve as the primary etiological factor for lens opacification, the resultant cataract may be referred to as "microwave cataract". Here the characteristic appearance and clinical course of the lens pathology are in a general way related to the intensity-duration function of and time interval between exposures. It is my practice to reserve the term, microwave cataract, for those cases which exhibit capsular opacification, a signature of radiation injury, after having had known, significant exposures only to the microwave portion of the electromagnetic radiation spectrum. (A similar clinical course can follow exposure, for example, to shorter or longer wavelengths where the diagnosis could be infrared or hertzian cataract, respectively).

At least three different stages or presentations of microwave cataract can be identified. Although they appear to be related to dosage, dose-rate and dose-interval, the relationships are not clear-cut. Transitions between stages are not distinctly demarcated probably because both cumulative and additive effects are contributing to produce a variable pathogenic evolution. Nevertheless, microwave cataracts can be classified as either (1) acute, (2) subacute or (3) delayed. Although this is not an entirely satisfactory method for describing all the permutations, it does serve to facilitate understanding of the findings as actually encountered in clinical practice.

Before describing the classification, it is necessary to provide some pertinent information about the normal lens and cataract formation. The lens is a mostly transparent biconvex tissue, measuring about a centimeter in equatorial diameter and about one half a centimeter in axial depth. It is located near the front surface of the eye immediately behind the iris so that its anterior surface is about one half a centimeter from the corneal surface. It is surrounded by a thin elastic membrane capsule perhaps averaging about 10 microns in thickness in the living eye. Because of its thinness and almost total transparency, the capsule is not easily detectable by slit-lamp examination. On the other hand, the normal lens substance, when viewed by slit-lamp biomicroscopy, has an observable relucency of the light beam so that it does not appear to be optically empty but, instead, it can be examined readily and much detail can be recognized. Further, the light beam relucency is not uniform throughout the lens substance but, instead, regions of optical density differences are apparent permitting a gross division of the peripheral portion, the lens cortex, from its central portion, the lens nucleus.

In addition, the slit-lamp magnification readily permits identification of small lens substance imperfections such as granules, vacuoles, precipitates and sutural markings. These are frequently referred to by ophthalmologists as opacities without much further description and the differentiation between capsular and contiguous cortex opacifications is seldom noted but, instead, pathology at this site is ordinarily described as subcapsular opacification.

Opacification can be present without a measurable reduction in visual acuity. The term cataract has been used often in the literature for localized regions of opacification which do not significantly interfere with vision. However, I prefer that its use should be correlated to the clinical relationship of visual function. In this context a cataract may be considered to be mature when it prevents any useful vision, immature when vision is partially present and incipient when disturbance of visual discrimination has just become apparent. This is the criterion by which I further define microwave cataract and differentiate it from microwave injury, an earlier stage of capsulopathy without any effect on vision.

In my experience and by my definition, all pure cases of microwave cataract must exhibit capsulopathy. Without capsular opacification I would not consider microwaves to be the primary etiologic agent. This is not to say that microwaves would not be contributory in accelerating the cataractogenic process for the usual types of cataract, all of which take origin in the lens substance. Thus, in hereditary, congenital, hormonal, toxic, metabolic, ionizing radiation or senile cataracts, microwave irradiation does not ordinarily produce or superimpose a new kind of cataract but, instead, it acts as a secondary, contributory or synergistic agent by shortening the time interval required for maturation.

Regarding microwave capsulopathy, it is not born fully formed. Instead, it ordinarily begins insidiously. The earliest recognizable stages are usually found at the posterior lens surface where it appears as if small, scattered regions of the capsule are roughened and thickened. Although it does take proficiency in the use of the slit-lamp to identify this finding, when the next stage, opacification of these regions of the capsule, commences, ordinarily this is readily observable if searched for. Once established, capsular opacification is irreversible. With the passage of time, additional loci appear and, depending upon the number, relative location to each other, degree of confluence and relative density of the opacification, which can vary from light gray to dense white, the capsular opacification can acquire a variety of localized forms. In some instances these give rise to a honeycomb, brush-mark, lace-cloth, spider-web, breadcrumb or peppered-surface appearance. Although the honeycombed configuration can usually be recognized, it is not uncommon ultimately to find variations of all of these descriptive appearances as more and more areas of the capsule become involved and adjacent areas coalesce. Eventually, as these areas become larger and denser, there can arise gross plaque-like or sheet-like areas having millimeter dimensions. At no time, however, does the entire lens capsule become uniformly or homogeneously dense white but instead, even when capsular opacification involves practically the entire lens surface some areas of clear capsule can still be recognized.

Although capsular opacification precedes lens substance opacification, the former does not become complete before the latter commences. Indeed, visual acuity does not diminish to any measurable degree until the lens substance has started to become cataractous. Further, the subsequent reduction in visual acuity varies directly with the site and quantity of lens substance pathology. For this reason, a brief description of the lens substance changes ordinarily associated with microwave cataract is in order. Many of the same lens substance processes are also associated with cataracts due to other causes.

Due to its avascularity and the barrier against penetration by wandering cells afforded by the capsule, the ordinary processes of inflammation and tissue repair after injury, which would be termed phakitis, cannot occur in the lens. However, the intact capsule acts as a Donnan's membrane so that water, for example, as well as some ions and solutes can pass through. When the lens substance imbibes fluid it can become edematous (hydrated) and this results in a swollen physical state (intumescence). This could be termed phako-hydritis and it can either be localized to a microscopic region of the lens giving rise to vacuoles, a minute macroscopic region giving rise to vesicles, a larger portion of the lens substance recognized grossly as a limited region of altered translucency or it can involve practically the total lens substance, producing a swollen appearance of the entire lens.

Phakohydritis is reversible providing its duration is brief or its extent is not massive. For example, if a single vascuole is present, a not uncommon finding in any lens, usually it will disappear completely, occasionally what appears to be a microscopic sharply demarcated precipitate remains behind for a period of time and subsequently, this too, ordinarily will be resorbed and disappear after a few months have elapsed or rarely a permanent minute microscopic coagulate will persist. However, when vesicles have formed, these persist for long periods of time and should they be resorbed they almost always result in some permanent coagulation of the contiguous lens substance appearing as a macroscopic imperfection or dot when the lens is viewed by ophthalmoscopy. When a sector or a gross portion of the lens exhibits altered relucency due to diffuse hydration it is usually visible to direct view, if it persists from weeks to months it almost always will result in some permanent degree of opacification and usually the opacification becomes denser with time. When the entire lens is intumescent and the hydration persists for more than one to two weeks, then the lens will become cataractous rapidly; this is a rare fulminating type of cataract which can be referred to as "hydrops" of the lens.

In the name of science (?), some unrelated ophthalmological conditions which cannot conceivably be mistaken for microwave cataract have been offered to raise questions about this clinical entity. For example, cataracta complicata and congenital capsular cataract have been such offerings. Cataracta complicata, also known as complicated cataract, arises secondary to inflammatory and degenerative changes in the retinal or uveal tissues and results from the release of toxins into the intraocular fluids. As the toxins diffuse into the lens they produce a polychromatic lustre at the posterior capsule and a rosette type cataract. At no time, does microwave cataract exhibit either polychromatic granules or polychromatism of any sort at the posterior capsule nor does it produce rosette cataracts.

Congenital capsular cataract is a rare, freak medical curiosity. When present, it is incompatible with useful vision and associated with other concomitant intra-ocular anomalies. The lens is smaller than normal, deformed and surrounded by an opaque, membraneous mesodermal sheath instead of a capsule. At no time can this be mistaken for capsular cataract.

CLASSIFICATION OF MICROWAVE CATARACT

1. The "acute" cataract rarely occurs in man. Although it could conceivably follow a single massive exposure, and thereby resemble most of the reported animal experiments, I do not yet know of such a human case. Instead, the typical acute microwave cataract has a history of repeated, short duration exposures, for example, from looking into a generator cavity to observe the color of the grids or to view an antenna

rotary joint for arcing through a hole cut into a waveguide. Ordinarily, the time duration of each individual exposure is estimated in seconds to minutes and repeated exposures vary from many times daily to several times per week during a period of weeks to months. Under these conditions, vision usually begins to fail during or immediately following these exposures. In addition to diminution of vision, which is ordinarily the chief complaint bringing the patient to the ophthalmologist, occasionally other ocular symptoms related to an irritable eye also develop. None of the patients reported sensing heat during any of the exposures.

The ophthalmological findings at the first examination are striking and vary from acute hydrops of the lens to an advanced stage of capsulopathy. Regarding the capsulopathy, ordinarily the posterior region of the capsule is more involved than the anterior region and some lens substance cataractogenesis, even though it may be minimal at this time, is evident. Within months to years, even if no further exposures take place, a practically complete capsular cataract will form and subsequently or simultaneously the lens substance also will become completely cataractous.

When a fulminating hydrops of the lens occurs, an inflammatory panophthalmitis occurs with evidence of keratitis, blepharo-conjuctivitis, iridocyclitis and chorioretinitis, leading to a stormy post-irradiation clinical course. In such a case, the contralateral eye may also develop a secondary uveitis. In some features, this contralateral uveitis resembles sympathetic ophthalmia except that it is less severe and more responsive to anti-inflammatory therapy than the primary radiation uveitis in the exposed eye.

2. The "subacute" microwave cataract ordinarily results from frequently repeated subclinical exposures carried out over a duration measured in months to years. Usually, the patient's only complaint is gradually failing vision. As a rule, there is a clear-cut history of intimate daily contact with a microwave source. Although some evidence of pathology is usually present in both eyes, it is seldom equal or bilaterally symmetrical. These cases are the most instructive so far as following the clinical course of microwave cataract is concerned because the two eyes present different stages of the injury and in follow-up examination of these cases the frequently observed latency and delayed evolution of microwave cataract can be determined. Further, when the source becomes identified, the patient can be spared from additional irradiation. By following the clinical course of such patients, the latency and slow progression of the cataract becomes evident as well as the fact that regression of the capsulopathy never occurs although it may remain at an arrested stage of development for long periods of time.

In a typical case, the patient, unaware of having been irradiated, is surprised to learn that the gradual almost imperceptible reduction of vision he has experienced over the course of a few months, predominantly in one eye, is due to an incipient cataract. He is further surprised to learn that his other eye has evidence of lens opacification. Unless a radiation etiology is suspected and the source identified or, for some other reason, such as changing job assignment, the covert exposures cease, the cataractogenic process will progress slowly but continuously in both eyes, and result in mature cataracts being formed over a period of several months to a few years.

Where the chronic exposures have been terminated, the rate of cataractogenesis frequently becomes reduced and may even appear to be arrested for many months or years. However, ordinarily this is only an apparent latency and the incipient cataract is not really dormant but, instead, it is developing at such a reduced rate that it takes years before becoming mature. Interestingly, in many of these cases, the cataract will spread along the capsule and remain localized to the capsule and contiguous cortex, almost completely surrounding the lens without producing opacification in the remaining bulk of the lens substance. As such, it is frequently referred to by most ophthalmologists as "capsular cataract". Subsequently, the entire lens substance will also become opacified although this may take many additional months or years.

3. The "delayed" microwave cataract usually forms insidiously over a five to thirty year period. The best documentation for this has been found where the contralateral eye has a subacute microwave cataract. Here, there is real latency as the capsulopathy frequently lies dormant for many months at a time. In the early years, progression, which occurs intermittently, is ordinarily recognized by additional areas of capsule becoming opacified. Eventually, lens substance opacification will ensue, either in the manner already described or by the intervention of nuclear sclerosis. Ordinarily the nuclear sclerosis form of cataract is considered to result from the aging process. However, I have found it to occur prematurely and follow an accelerated course in the presence of microwave capsulopathy.

REPORT OF CASES

Case 1. Mr. C. J., a 44 year old white male. At age 27 while working as a microwave researcher, he performed an experiment testing the function of a radar rotary joint by watching for arcing through a small hole cut into the waveguide. He performed this task intermittently on several different days during a three to four week period. On the testing days, the task was repeated many times. Each viewing lasted from seconds to a minute or two in duration. All the viewing was performed with the right eye. Although the highest possible calculable exposure field strength to the right eye could have been 4 W/cm², it is more reasonable to estimate that his exposures averaged about 500 mW/cm². His work was interruped because the vision of his right eye failed rapidly. Ophthalmological examination revealed that he had an acute, fulminating microwave cataract and panophthalmitis of his right eye. Within a few weeks, he developed a mild uveitis of his left eye. The bilateral uveitis responded to anti-inflammatory therapy within a few months and has not recurred.

Seven years later, a cataract extraction combined with sector iridectomy and anterior and posterior synechiotomies was performed on the right eye. During this seven year period, the patient developed a few microscopic areas of capsular opacification at the posterior surface of the left lens and a 0.1 millimeter thick linear streak of pigment, subtending an arc from 4—8 o'clock, also became prominent on the posterior surface of the lens. During the next ten years, the capsulopathy gradually increased in size, in number of loci and in density of opacification; however, the visual acuity can still be corrected to 20/20 although the patient states that his vision is not sharp. Also, during this time, the trabecular region of the eye and the posterior surface of the cornea have gradually become pigmented and degenerative changes have occurred in the corneal endothelium and peripheral retina. Perhaps most significantly, recently the streak of pigment containg cells on the posterior surface of the lens appears to be undergoing active growth. It has extended to encompass practically the entire equatorial region of the lens. At each end of the original pigmented streak, there is now a further suggestion of cellular activity as these regions have enlarged and appear like satellite colonies. The medial end is now circular with a diameter of 1.0 millimeter and the lateral site is oval and measures about 1.0 × 3.0 millimeters. Technically, the diagnosis is melanoma and the question to be resolved is whether it is completely benign or will become malignant.

Several years ago the patient developed degeneration of an intervertebral disc in the lumbar region requiring spinal fusion but, otherwise, he has been in good general health.

Case 2. Mrs. B. L., a 51 year old white female. The patient had been in excellent health throughout her life and the only history of potential radiation exposure was that she used a consumer type microwave oven regularly for five years between 1966 and 1971. Because of her failing sight due to cataracts of an unusual type, the oven was tested in 1971 and found to be leaking at a maximum level of 2.0 mW/cm² during operation and 40.0 mW/cm² when the door was opened. The oven was not used afterwards but it was retested in 1972, at which time it was reported to be leaking microwaves at a level of 1.0 mW/cm² during operation and 90 mW/cm² when the door was opened. Her exposures were covert and occurred between 1966 and 1971.

In prior years, her eyes were examined and found to be completely free of disease. In June 1969, because of a sense of blurred vision of the right eye, she was examined by her ophthalmologist who reported that although her visual acuity could be corrected to 20/20 in the right eye and 20/15 in the left nevertheless incipient opacities were forming at the posterior subcapsular area of both lenses, being more pronounced in the right eye than the left. The cataracts progessed so that by April 1972 it was necessary to perform cataract surgery for the right eye and the best refracted vision of the left eye had been reduced to 20/50. The patient was referred to me for consultation in February 1973 and she had the typical findings of subacute microwave cataract in her left eye.

Case 3. Mr. A. K., a 44 year old white male. At age 21, he served in the United States Navy during the Korean War as a radar maintenance man. For about a year during 1950 to 1951 he was exposed repeatedly to microwave radiation from patrol aircraft radars at field strengths up to a maximum of 1.0 W/cm². I first examined the patient in 1964 when he was 35 years old and his ophthalmic findings were immature subacute microwave cataract of the right eye and a minimal stage of delayed microwave cataract of the left eye. During the next nine years, the cataract of the right eye has progressed slowly but steadily so that now it involves practically the entire capsule and most of the contiguous lens cortex. The central portion of this lens remains clear so that it can now be classified clinically also as a capsular cataract. There has been very slight progression of the posterior capsulopathy in the left eye which can still be corrected to 20/20 visual acuity.

Since being discharged from the Navy, the patient has had episodes of mental illness, cardiovascular disease with depressed and inverted T waves, osteoarthritis and thyroid dysfunction.

Case 4. Mr. D. B., a 41 year old white male examined by me in 1968. He was identified only as a member of a large group of researches working with microwaves at field strengths lower than 10 mW/cm². He was a participant in a screening examination designed to identify microwave injury. His examination revealed the typical microwave-induced honeycombed opacification of the posterior capsule in both eyes. As the involved areas were large, about 3 millimeters in diameter for the left eye and 2 millimeters in diameter for the right, and inert because there was very little opacification of the contiguous cortex, the diagnosis was an early stage of delayed microwave cataracts. During the previous year, the patient had undergone surgical removal of a testicular malignancy.

Case 5. Mr. J. F., a 44 year old white male. The patient was first examined by me in 1971, when he was 42 years old, because he had been advised that he was developing microwave cataracts. Examination revealed extensive capsular cataract of the left eye, a late stage of subacute microwave cataract with beginning exfoliation of the capsule and a suspicion of posterior synechiae (which was confirmed at surgery) and an early stage of delayed microwave cataract in the right eye.

The patient had worked on several different radar systems from the time he was 26 years old until he was 35 during the period from 1955 through 1964. The highest field strength to which he was regularly exposed was about 1 mW/cm² for durations up to three hours and occasionally he could have been exposed to field strengths up to about 25 mW/cm² for a minute or less.

The patient fathered a son, born early in 1964, the product of a normal pregnancy, who did not appear as alert and did not develop as rapidly as other children. The child sat at six months, stood at twelve months and walked at eighteen months. About that time, brief head nodding developed which progressed to a form of psychomotor epilepsy, subsequently exhibiting symmetrical clonic movement of all extremities and the eyes lasting a few seconds and finally he exhibited lethargy. The boy died at age 7 and autopsy revealed that he had a rare, most unsual degeneration of his thalamus.

Case 6. Mr. M. D., a 50 year old white male. At age 49 the patient was referred for a consultation because he had a cataract in one eye and he had worked as a radar engineer since 1951. Examination revealed a minimal microwave capsulopathy at the posterior surface of both lenses and advanced nuclear sclerosis of the right lens without any trace of nuclear sclerosis in the left lens. Vision in the right eye could not be corrected to better than 20/400 while it was 20/20 in the left eye. Prior to 1970, when he was discovered to have a nuclear sclerosis type of cataract in his right eye, his vision was excellent in both eyes and no ocular pathology had ever been noted previously.

The patient's occupational history was reliable. The only work assignment that could have led directly to exposure occurred 20 years previously when for 18 months he was employed testing magnetrons. This assignment involved viewing the cathode emitter through a small hole via a mirror arrangement. All of the viewing was performed with his right eye. The maximum exposure was estimated to be at a field strength no higher than 1 mW/cm^2. The diagnosis was delayed microwave cataract of the right eye and delayed microwave injury of the left eye.

In March 1973 the patient sustained a cerebrovascular accident secondary to occlusion of the right internal carotid artery. Emergency surgery, endarterectomy with resection of atheroma and plastic revision of the artery were performed successfully and the patient is making a slow recovery from the cerebrovascular accident.

Both sites of delayed appearing pathology, the right eye and the right internal carotid artery, were located within the zone being irradiated while the patient was viewing the magnetron cathodes.

DISCUSSION

Each of the case reports has prima facie evidence of microwave injury, i.e., a clear history of inhabiting microwave environments and the signature radiation cataract. In addition, each case exhibits in at least one eye, the covert nature of exposure, the long duration latency and the slow evolution of pathology typically found in man.

These cases have been selected from a reservoir of more than 50 patients having primary microwave cataract. They signify clearly that most of the previously collected experimental microwave cataract data are inappropriate, inapplicable and unsuitable either for the understanding of the disease process as it ordinarily occurs in humans or for the formulation of permissible levels of irradiation. Perhaps the most important and significant finding in this regard is the pre-senile appearance of nuclear sclerosis of the lens which indicates that the aging process may be initiated prematurely or accelerated by microwave irradiation.

Aside from premature aging, there are a number of other microwave bio-effects that have been reported in both animals and humans, such as ocular, testicular, embryological, cardiovascular, neural and endocrine disorders. Although microwave lens injury is common to all the cases I have reported, each has additional findings which could be attributable to irradiation.

Among the ophthalmological findings are hydrops of the lens, kerato-conjunctivitis, irido-cyclitis and chorioretinitis which can develop immediately following irradiation. At a later date, keratopathy, capsular exfoliation, synechiae, glaucoma, retinal degeneration and melanomata can appear. After years of latency, endothelial dystrophy of the cornea and nuclear sclerosis of the lens, indicating premature aging, also can appear. Further, because the capsule is weaker and there is a greater likelihood of adhesions between the lens and the adjacent iris anteriorly and vitreous posteriorly than with most other types of cataracts, the surgical extraction of microwave cataracts carries a higher complication rate and requires greater than ordinary skill in order to minimize surgical complications.

Non-ophthalmological findings observed in this select group of cases include mental illness, cardiac, vascular, hormonal and arthritic disease and testicular malignancy. In addition, one of the subjects, after many years of chronic exposure to microwaves, fathered a child with a rare bizarre, fatal central nervous system degeneration.

The mere chronicling of these case reports provides a grim picture. This is particularly true when it is coupled to the protean nature of the electronic smog pollution problem. In this context, let us consider only our background microwave habitat. The solitary significant natural source is the sun. Under worst case conditions (sunburst activity), the integrated sum for the entire microwave bandwidth produces a field strength less than 1×10^{-8} mW/cm^2. In this regard, there is not much difference between western or eastern oriented standards and nothing about either that can be recognized as being safe. For example, the west emphasizes avoiding a burn while the east desires to prevent a simmer. Both imply that a vacation from the microwave environment is curative. Neither has faced up to the real problem identification and prevention of the late or delayed appearing radiational effects.

RETINAL CHANGES IN MICROWAVE WORKERS

B. Tengroth and E. Aurell

Department of Ophthalmology, University of Gothenburg, Gothenburg, Sweden.

The cataractogenic effect of exposure to microwaves has been reported by several authors. Effects on the central nervous system have also been discussed. It is unknown whether the effect is thermal or nonthermal in origin. In this paper the authors show that in a factory where radar and other microwave equipment was tested an over-representation of lens opacities could be observed in personnel in the lower age groups. Furthermore it was noted that changes in the retina resembling chorioretinal scars were present in a significant number of workers.

During the last quarter of a century there has been a marked development and increased utilization of devices that emit various forms of non-ionizing radiant energy, including equipment for industrial and medical applications as well as for military use. Microwaves have come into use primarily in the military field but also for short-wave diathermy medical therapy and for domestic use in cooking. Today microwave emitters are widely spread. The electromagnetic radiation characterized as microwaves has a wavelength between 0.3 mm and 300 cm corresponding to 10^8—10^{12} Hz. The microwave energy can be propagated either pulsed or as a continuous wave (CW).

Where the microwaves are absorbed they give an increased kinetic energy to the molecules exposed, which will increase the possibility of collisions between molecules and hence result in increased temperature in the entire material.

The biologic effects of microwaves have been very thoroughly investigated in many places but especially in the Triservice Program (5). There is general agreement that the effect of microwaves in tissues is mainly of thermal origin. However, non-thermal effects have been suggested and there is still a great deal of controversy on this subject.

One of the most throughly investigated aspect of the pathologic effects of microwaves is the denaturation of lens proteins resulting in lens opacities — cataract (2, 3, 6, 7). General effects on the central nervous system, i.e. headache and nausea, have been reported from the USSR, but it is still a matter of dispute whether these symptoms are secondary to temperature increase in the organism or direct non-thermal effects on the nervous tissues. In most industries and military organizations involved in microwave work yearly controls of their personnel are recommended, especially checking of the eyes. In one of the industries working with radar equipment such check-ups started quite recently. The preliminary findings were rather astonishing in two ways; first, the frequency of significant lens opacities in the younger age group was greater than expected and secondly, retinal lesions in the paramacular and macular region were observed in a number of cases, with decrease in vision in two cases. As retinal lesions have never been reported in the literature as far we have found, an epidemiologic study was performed, in order to find out whether the above-mentioned changes had any significance.

MATERIAL

98 employees in an electronic industry developing radar equipment were investigated. 68 had been exposed to microwaves for a certain time or were still working in this field. This group could be divided into persons testing radar equipment and measuring microwave radiations from different klystrons and persons from the experimental laboratories. A control group of 30 persons from the same industry was exposed to microwave radiation, as far as was known.

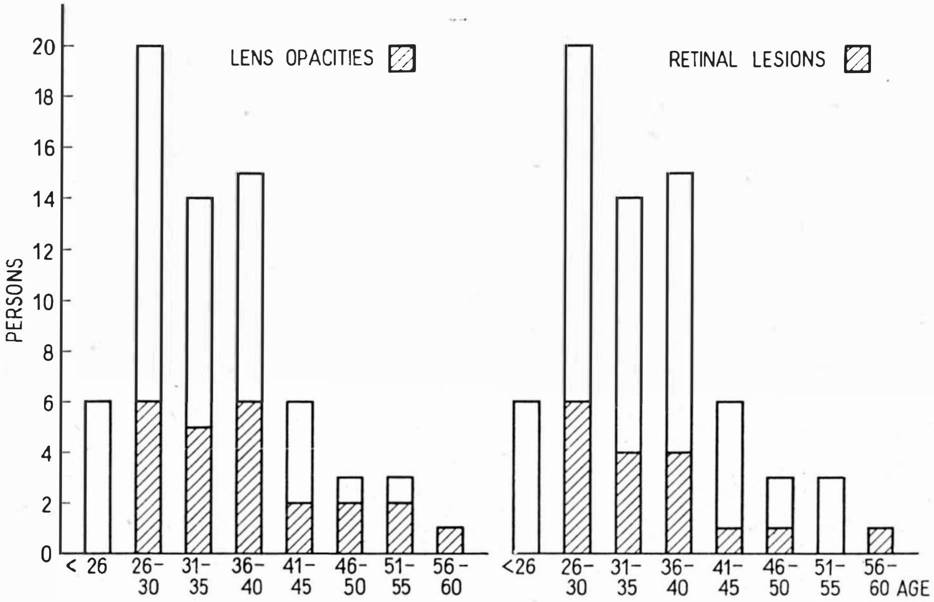

Fig. 1. Exposed persons (68 cases).

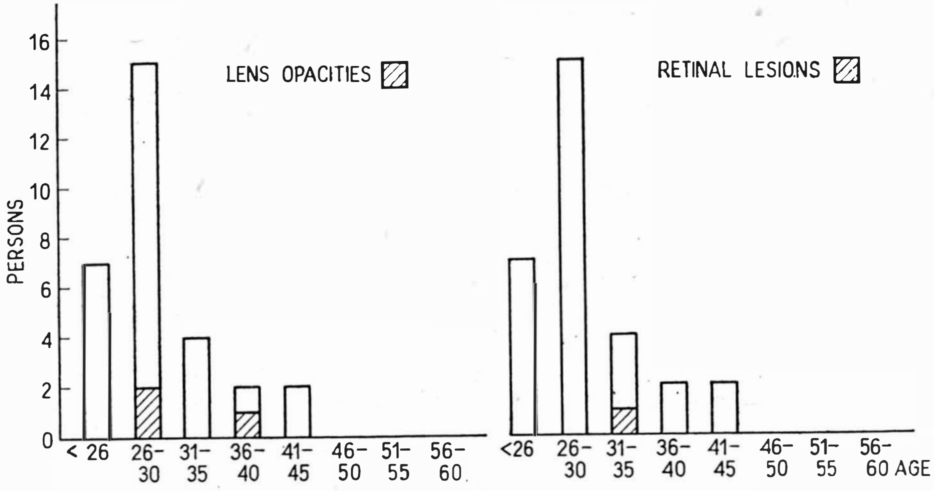

Fig. 2. Controls (30 cases).

METHODS

Two eye specialists independently made a careful eye examination of all personnel mentioned above without any knowledge of their occupation or microwave exposure. The examination included determination of refraction and visual acuity, a study of the optic media with the aid of a corneal microscope and slit lamp in complete mydriasis, and a study of the retina with an ophthalmoscope.

DEFINITIONS

Only lens opacities of a diameter of more than 0.5 mm or a high concentration of smaller opacities in the subcortical region were taken as significant. Very small opacities spread out in the lens were not recorded. The opacities should be detectable also in the ophthalmoscopic media examination. Retinal lesions were looked for only in the central part of the fundus and were characterized by their resemblance to chorioretinal scars after inflammatory reactions. Small yellow changes in this region were also observed and recorded but were not classified as lesions of significant importance.

RESULT

As can be seen in the diagram the number of exposed subjects with lens opacities is high, even in the younger age groups. Only in two cases was there disagreement between the examiners and these two cases from the exposed group were excluded from the material. In the higher age group — above 41 years — it was impossible to separate lens opacities due to microwave exposure from a senile cataract because no controls were examined.

Retinal lesions, hitherto never reported, are also of high frequency. Only one case was found in the control group, which makes the exposed group significantly different. Dividing the group of exposed personnel according to their tasks (testing personnel — laboratory personnel), one can observe a concentration of lens and retinal lesions in the former.

DISCUSSION

It is of great interest that eye lesions, both lenticular and retinal, were found in this material significantly more often in persons belonging to the test group than in persons working in the laboratories. It is difficult to draw conclusions as to which kind of work is the most risky, but one knows that the personnel testing the equipment or measuring radiation are more apt to be exposed to higher power levels than others, i.e. laboratory personnel. This is of importance as the maximum permissible exposure (MPE) of 10 mW/cm^2 might be a figure that is too high — a comparison with the Soviet figures suggests this. Another explanation is that the eye lesions observed are due to leakages from the equipment or carelessness of the personnel. As we have a concentration of damaged persons in a certain exposed group the MPE is probably sufficient and the other suggestions more reasonable. The retinal lesions observed were earlier briefly reported by the authors (1). Since then we have been informed by a Polish scientist (4) that in a very recent study initiated by our findings similar retinal lesions were observed in personnel exposed to microwaves, which confirms our observations.

The pathogenesis of the retinal lesions is very obscure. The transmission properties of microwaves in biological tissues do not explain why certain areas in the retina should be changed as a result of thermal effects. The change in dielectric constants in the different layers of the retina might give an increase in intensity of three to four times between the layers but this seems too small an increase to explain the damage.

It is, of course, not known whether non-thermal radiation effects cause these changes. Further experimental and theoretical work has to be carried out in order to find the explanation. The most important findings reported here are the retinal lesions as these lesions have resulted in a decrease of vision in two cases. In no case known have the lens opacities resulted in a comparable loss of vision. In the future the necessity for a careful examination of the fundus of the eye has to be stressed and further experiments will hawe to be carried out as damage to such nervous tissue as the retina suggests that similar changes might appear in other kinds of nervous tissue after exposure to microwaves.

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ASSESSMENT OF LENS TRANSLUCENCY IN JUVENILES, MICROWAVE WORKERS AND AGE-MATCHED GROUPS

S. Żydecki

Institute for Postgraduate Study, Military Medical Academy, Warsaw, Poland

In recent years much attention has been paid to possible health hazards of microwave radiation. In the eye, the lens is considered particularly sensitive and divers changes have been described. Microwave changes in the lens are, however, the subject of controversy and opinions on the effects of occupational exposure differ. One of the reasons is that different criteria are used for the assessment of lens translucency.

The aim of this study was to establish criteria for evaluation of lens translucency and to examine it in individuals who did not have any contact with microwave radiation and in microwave workers. Taking into account exposure levels, age and duration of occupational exposure it should be possible to determine microwave effects in the lens.

3000 individuals of both sexes were examined. The whole population examined comprised 3 groups, 1000 persons in each. Group A comprised two subgroups. A_1 contained 542 individuals exposed directly to microwave radiation at power density about 0.1 mW/cm^2 and up 1 mW/cm^2. During short periods of time the mean power density could reach up to 6 mW/cm^2. Group A_2 comprised 458 individuals exposed to microwaves at 0.01 mW/cm^2 or less. All the persons examined were exposed on the average during 4 h daily, the history of occupational exposure ranging from 1 to 15 years. Several consecutive examinations were made in hospital (590 persons) or out-patient department conditions (410 persons). Group B comprised 1000 age-matched individuals not exposed occupationally to microwaves, while group C was made up of children and juveniles aged 5 to 17 years. Both groups B and C were subjected to a single examination in an out-patient department.

The examination of the lens was made using a slit lamp after dilatation of the pupil. Lens translucency was assessed using a 5-grade scale presented in Table 1.

The translucency of the lens was highest in group C and because of this, this group will be considered first. Grade 1 was found in 68.8% of cases on the average. Subdivision of this group into age-groups demonstrates clearly the influence of age, the incidence of grades 2 and 3 increasing between 10 and 17 years of age. Sporadic cases of grade 4 and 5 translucency confirm the fact that certain changes may be inborn (cf. Tab. 2). In comparison with group C, group B demonstrated worse characteristics of lens translucency, lenticular opacities increasing with age. Both groups, B and C, served as controls for group A, making it possible to determine both the frequency of inborn defects as well as defects appearing with age. A detailed analysis of these groups allows the conclusion that a close correlation (linear relationship) exists between age and the grade of lens translucency; the frequency of inborn defects may be estimated at about 0.7% (grades 4 and 5). Before a comparison with group A is made, it should be stressed that it was highly preselected, all individuals with grade 4 or 5

Table 1

Classification of lens translucency

Lens changes	Grade	Qualification as to fitness for microwave exposure
None	1	fit
Single, small, multishaped (dust-like points, radial striations) opacities, which may be counted; no visual acuity impairment	2	fit
Numerous small, multishaped (dust-like points, irregular, radial striations) opacities, which are difficult to count; no visual acuity impairment and no tendency to increase on successive examinations	3	fit to continue occupational exposure, should be observed; unfit as a candidate for admission to work or for training in a profession involving microwave exposure
As above, but with a tendency to increase in number or size on successive examinations	4	unfit
Any change impairing visual acuity	5	unfit

Table 2

Percentage incidence in various lens translucency grades in groups examined

Lens translucency grade	Group A			Group B	Group C
	A_1	A_2	A_1+A_2		
1	13.0	31.1	21.7	29.7	68.8
2	62.0	52.6	57.7	50.3	26.9
3	19.7	12.2	16.2	16.6	3.6
4	4.8	3.5	4.1	2.6	0.3
5	0.5	—	0.3	0.8	0.4

translucency being eliminated before admission for work in microwave exposure conditions.

Statistically significant differences in the frequency of various grades of lens translucency exist between group A and groups B and C. Moreover the comparison between subgroups A_1 and A_2 also demonstrates statistically significant differences. A more detailed analysis, according to the duration of occupational exposure, demonstrates that this does not play a decisive role. The decrease in lens translucency seems to depend rather on power density levels. If safe exposure limits are observed and single exposures remain below the permissible power density levels and respective exposure times per 24 h no effects on the incidence of lens opacities are observed.

It should be stressed that no particular morphologic features, distinguishing the lens opacities in microwave workers from those seen in the control population, could be detected. This may indicate that long-term overexposure to low doses of microwaves (below cataractogenic levels) may tend to accelerate the normal aging process of the lens. This indicates also that grade 4 lens translucency should be considered a contraindication for continuing occupational microwave exposure.

It should be stressed also that any case of cataract suspected of being due to occupational exposure to microwaves should be fully documented. Any other cataractogenic factors should be excluded and the results of earlier ophthalmologic examinations presented.

Session F. Presentation and Discussion of Session Reports, Conclusions (Including Future Research Needs) and Recommendations

Chairman: *C. Susskind*
Vice-Chairman: *J. C. Gallagher*
Rapporteurs: *K. V. Nikonova and E. Shalmon*

MICROWAVES — A TOOL IN MEDICAL AND BIOLOGIC RESEARCH

E. H. Grant

Physics Department, Queen Elizabeth College, London, United Kingdom

INTRODUCTION

When microwaves are incident on a medium a certain proportion of the incident energy will be reflected and the rest transmitted through the interface into the medium. This transmitted energy will be partly absorbed and the remainder will emerge from the medium without any interaction having taken place. For this latter radiation the medium is behaving as a transparent object. This simple picture is, of course, obvious but it does enable the problem of the degree of interaction of microwaves with biologic tissue to be broken down into two parts: For a microwave of a given frequency how much energy is reflected and how much energy is absorbed? These questions can, in principle, be answered if the angle of incidence and the complex permittivity of the tissue are known. In practice the former quantity is only known under well controlled experimental circumstances, e.g. if the tissue is contained within a waveguide or coaxial line, or for certain well defined free-space conditions. The complex permittivity of biologic materials can, however, be rigorously determined for a given sample and provided the sample can be taken as typical for the form of tissue which it represents, it should be possible in principle to build up a collection of data for the electrical properties of body tissues. There is one important property which most biologic materials possess and which enables this hope to be partially realised in practice. Most tissues have a high aqueous content and in the microwave frequency

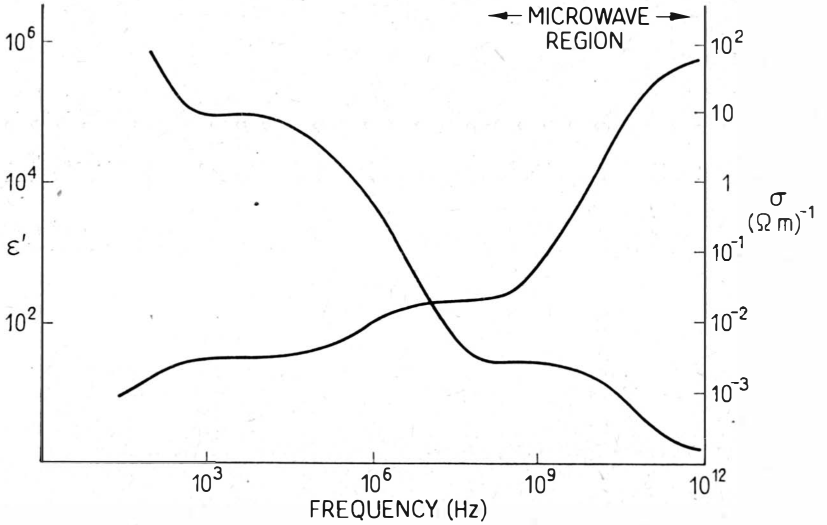

Fig. 1. Fall of permittivity (ε') and increase in conductivity (τ) with increasing frequency for a typical biologic tissue (the profile of the curve for the attenuation coefficient is similar to that for σ).

region (300 Mz—300 GHz) the electrical properties of water dominate those of all the other biologic molecules present. At lower frequencies this would not be the case: for example the electrical permittivity of blood at frequencies of a few kHz is equal to several thousand whereas at 3 GHz it is around 60. This situation is further illustrated in Figure 1 where it is seen that in the microwave region the electrical conductivity of a biologic solution increases by a factor of around 10^4 while the permittivity decreases by a factor of about 15. These changes are due almost entirely to the water content, and constitute the γ-dispersion. The β-dispersion is due to the biologic macromolecules and the δ-dispersion is usually regarded as being due to the bound water (11) or to the side-chains associated with the macromolecules or to a combination of both effects (19).

Thus if we know the dielectric properties of water between 300 MHz and 300 GHz we are able to predict roughly how a given biologic tissue will behave when subjected to microwaves of a specified frequency. According to this picture if the volume of a biological solution consists x% of macromolecules (e.g. nucleic acids or proteins) and (1—x)% of water then the values of the electrical parameters of the solution at a given frequency and temperature will be about (1—x)% of the values for the same parameters of water at the same frequency and temperature.

This approach, although giving a useful overall picture, can be criticized on several counts. It is known that the structure of the water immediately surrounding the biologic macromolecules in solution is different from that occurring in pure water, and there is good reason to think that the electrical properties of this "bound" or "modified" water may be different from those of pure water at the same frequency. Another consideration is the possibility of resonance absorption, which can be defined as selective absorption of energy in a narrow frequency band. The bound water phenomenon is well established and there is some evidence (20), (4) that resonance absorption could occur; both of these topics will be considered later in the paper. It can be stated at this stage, however, that for a proper understanding of the mechanism of absorption of microwaves in biologic material it is necessary to know the electrical permittivity and conductivity as a continuous function of frequency over as large a part as possible of the frequency region 300 MHz—300 GHz and at a temperature of 36.9°C. Moreover, it is not only the calculation of microwave absorption and the subsequent evaluation of microwave hazards which require the knowledge of these electrical parameters. They may be used in other areas of medical and biologic research, such as the investigation of the molecular aspects of hyperbetalipoproteinemia, the treatment of malignant disease by hyperthermia and the evaluation of the size and shape of biologic molecules in an aqueous environment. These and other aspects will be discussed later in the paper.

ELEMENTARY THEORY AND EXPERIMENTAL METHODS

The complex relative permittivity of a material may be defined by the expression

$$\hat{\varepsilon} = \varepsilon' - j\varepsilon'' \qquad [1]$$

where ε', the real part, is traditionally referred to as the dielectric constant while ε'', the imaginary part, is the dielectric loss factor. When an electromagnetic wave traverses a medium ε'' is a measure of the energy absorbed per cycle by the medium. Since the length of the cycles gets shorter as the frequency increases ε'' will eventually decrease to zero although the total energy absorbed by the medium is finite. Hence ε'' is not a realistic parameter for assessing energy absorption. A better parameter to use would be the conductivity $\sigma = \varepsilon''/\omega\varepsilon_0$ where ω is the angular frequency of the radiation and ε_0 is the permittivity of free space. It is well known from simple electromagnetic theory that the energy absorbed by unit volume of a medium in unit time is related $\sigma E'$ where E is the strength of the electric field. Even this expression is not applicable to a microwave passing through an absorbing medium such as a biological tissue, however. This is because the field strength is not constant throughout the medium but diminishes due to attenuation. Thus if a microwave with an electric field strength E_1 is attenuated from E_1 to E_2 by a width x of tissue then $E_2 = E_1\exp(-\alpha x)$ where α is the attenuation coefficient of the medium at that particular frequency. Hence the energy absorbed is proportional to $1 - \exp(-2\alpha x)$. The relationship between α and the complex permittivity for a TEM mode is given by

$$\alpha = \frac{2\pi f}{c}\left[\frac{(\varepsilon'^2 + \varepsilon''^2)^{\frac{1}{2}} - \varepsilon'}{2}\right]^{\frac{1}{2}} \qquad [2]$$

where S is the microwave frequency and C is the velocity of electromagnetic radiation *in vacuo*. This makes the relationship between absorbed energy, the frequency and complex permittivity a fairly complicated one. When α is small, however, $1 - \exp(-2\alpha x)$ tends to $2\alpha x$ which when combined with suitable approximations to equation [2] shows that the absorbed energy is proportional to α in this limiting situation, or to σ. This corresponds to the low-frequency end of the dispersion region and therefore approximates to the well known case of a medium between the plates of a condenser where simple theory indicates that absorbed energy is proportional to conductivity. In general, however, it must be emphasized that the parameter determining energy absorption is the attenuation coefficient α. The variation of α with frequency is a similarly shaped curve to the corresponding variation for conductivity shown in Fig. 1 in that it starts at a low value and attains a plateau at the high-frequency side of the dispersion region.

The relationship between the energy reflected from the interface of the medium and the dielectric parameters is also complicated but to a first approximation is proportional to

$$\left[(\varepsilon')^{\frac{1}{2}}-1\right]^2\left[(\varepsilon')^{\frac{1}{2}}+1\right]^{-2} \qquad [3]$$

if the wave is incident from air. Thus in view of the rapid changes of the complex permittivity throughout the microwave region for a biologic material, the importance of knowing ε' and ε'' (and hence α) accurately at each frequency of interest is seen.

Techniques for measuring $\varepsilon = \varepsilon' - j\varepsilon''$ for lossy liquids at microwave frequencies fall into three main categories. These are resonance methods, standing wave methods and traveling wave methods. Resonance methods have been used by Schwan (22) to measure the permittivity of a wide range of biologic solutions (23) at frequencies up to 1 GHz. At higher frequencies the increasing conductivity (Fig. 1) causes a rise in the energy absorption and the resonance type of method becomes less sensitive although methods have been used recently at 2.6 GHz using waveguide cavity resonators (e.g. Masszi (17) and Almassy (2)). Techniques using a movable probe in a coaxial line have been employed by Buchanan and Grant (5) and have been subsequently developed by Pennock & Schwan (19) by Grant and Keefe (10) by Jordan (16) and by Sheppard (25), (26). These have worked satisfactorily from 300 MHz up to 4 GHz and are currently being extended to 8 GHz. At higher frequencies the waveguide bridge method as described by Buchanan (3) or by Grant and Shack (12) must be used.

RESULTS

We have been studying the electrical behavior of biologic solutions for the past twenty years at the Middlesex Hospital Medical School, Guy's Hospital Medical School and during the last seven years at Queen Elizabeth College, London. Some of this work has been carried out in collaboration with other centers; in particular with Portsmouth Polytechnic, the Department of Biomedical Electronic Engineering at the University of Pennsylvania, the Courtauld Institute of Biochemistry and the MRC Clinical Genetics Unit at the Institute of Child Health, London and with the Simon Stevin Institute at Bruges, Belgium. Substances measured include aqueous solutions of hemoglobin (15), myoglobin (27), ribonuclease and serum albumin (9), whole blood, lipoproteins (14), smaller biologic molecules typified by various amino acids (23) and peptides (1), and water itself (13). The results have been described in various publications, some of the principal ones being listed at the end of this paper. To cover the three principal dispersions (Fig. 1) measurements have been made from a few kHz up to 35 GHz. Since, however, this Conference is only concerned with the frequency region 300 MHz — 3000 GHz the β-dispersion is not relevant. One recent study has been concerned with the permittivity of whole blood at 2 GHz for various concentrations of hemoglobin. In another experiment the dielectric properties of solutions of LDL lipoproteins taken respectively from normals and from patients with hyperbetalipoproteinemia have been measured at 800 MHz and significant differences found (14). In a third study the dielectric behavior of water has been measured between 400 MHz and 4 GHz (13).

The results of the first two studies will now be described briefly. Blood is composed of living cells and plasma, a heterogeneous mixture of molecules of which the majority are polar. The dielectric behavior of blood has been studied previously by Schwan

(21) and Cook (7) and as a result of this work it is known that the dielectric constant falls from a few thousand at radio frequencies to about 60 at about 300 MHz from which it then falls through the microwave region to a value of between 4 and 5 at 300 GHz. This variation follows the typical pattern shown in Figure 1. The high value of E′ at low frequencies is due to the red cell membrane and the rotation of polar macromolecules. In the microwave region the permittivity is, as expected, due mainly to the free water molecules. Hence any variation in ε' due to changes in the concentration of red cells or serum proteins should be due solely to changes in the relative proportion of the volume occupied by free water. We have tested this hypothesis by measuring the permittivity at 2 GHz of blood of different hemoglobin concentrations. Five samples were measured of hemoglobin concentration (c): zero (pure serum), 4.1, 6.8, 9.1 and 15.0 mg/ml, the final concentration corresponding to blood from a healthy person. The values of ε' at 2 GHz and 23.6°c were 70.0, 66.4, 64.3, 62.6 and 58.0 respectively. This result shows a linear relationship between ε' and C and proves that, at microwave frequencies, the contribution of the hemoglobin to the permittivity is small and is negative, i.e. it has its effect by displacing free water molecules. The proportionality between permittivity and hemoglobin concentration is interesting and could form the basis of an alternative method of measuring hemoglobin concentration.

The second application of dielectric methods is in the field of lipoproteins. There is a strong association between the incidence of coronary heart disease and the concentration of cholesterol in the serum. Furthermore, for cholesterol concentrations greater than 325 mg/100 ml the risk of dying from coronary heart disease is ten times greater if the hypercholesterolemia is caused by the mutant gene for familial hyperbetalipoproteinemia. It would therefore be very useful if the genetically determined form of the disease could be distinquished from that which is due to environmental causes. We have measured the dielectric constant (ε') of aqueous solutions of low-density lipoproteins of density range 1.007—1.063 g/ml (LDL). The measurements were carried out at 800 MHz in a coaxial line and at 20°C. Blood samples were obtained by venepuncture from three normals (N), two heterozygotes (He) and one homozygote (Ho). The mean values of permittivity were 72.77 ± 0.17, 72.36 ± 0.14 and 72.01 ± 0.19 for N, He and Ho respectively at a concentration of 61.0 mg/ml of lipoprotein in water. These were interpreted by a simple mixture formula in terms of the hydration (bound water) to give the hydration ranges of 0.00—0.06, 0.07—0.11, 0.11—0.17 g lipoprotein/g water for N, He and Ho respectively. The ranges correspond to the 95% confidence interval. Thus the results of this pilot study (14) show significant differences in the hydration (w) between the normals and both types of familial hyperbetalipoproteinemia. This work is now being extended to include larger numbers of subjects in each category.

The values of w for the lipoprotein are much smaller than those obtained for globular proteins but this could partly be attributed to the fact that a given macromolecule might be expected to bind a certain layer of water rather than a certain mass. In this case the hydration factors would tend to be larger for the smaller molecules and vice versa.

DISCUSSIONS AND CONCLUSIONS

It has been assumed for some considerable time that the degree of reflection and absorption of microwaves by a biologic tissue is mainly determined by the value of the complex permittivity of water at the frequency in question. In my view some important practical and clinical implications are going to be missed if this simple picture is accepted without reservations.

In the second example cited in the previous section the dielectric behavior of the bound water is seen to be quite different from that of the free water. There is still a great deal to be discussed about the dielectric behavior of protein-bound water but most workers (11, 19, 28) agree that its relaxation frequency lies between 100 MHz and 1 GHz. The static (ε_s) and infinite frequency (ε_∞) permittivities of bound water are not yet known with much precision but since for ice ε_s is only a few percent higher than ε_s for free water the value for bound water is unlikely to be very different. The same goes for ε_∞. These facts can now be applied to a situation of practical interest.

At the temperature of the human body the relaxation frequency of pure water is 26 GHz which is therefore about ten times greater than the operating frequency of a microwave oven which, in turn, could be about ten times greater than the relaxation frequency of bound water. Assuming this to be so and assuming that ($\varepsilon_s - \varepsilon_\infty$) is the same for free and bound water it can be calculated from equation (2) that the attenuation coefficient (α) of bound water at 2.45 GHz is about three times as high as that of free water. Since it is α that determines the energy absorption and since, also, the bound water molecules are immediately adjacent to the biologic molecule being damaged the importance of knowing the dielectric parameters of the bound water as well as the free water is abundantly clear.

The possible role of bound water in relation to genetically induced hyperbetalipoproteinemia has been explained above. Another area of clinical interest is the treatment of cancer by hyperthermia. It has been shown by Cavaliere (6) and others that malignant cells are more susceptible than normal cells to damage from thermal stimuli. Temperatures of between 41.5°C and 43.5°C are usually involved in these studies. Recently Overgaard and Overgaard (18) have used electromagnetic waves of 27.12 MHz to treat mammary carcinoma in mice by hyperthermic action and, on the more fundamental side, Drost Hansen (8) has suggested that the effectiveness of hyperthermia therapy may be due to structural transitions in the water associated with the cells at 45°C. The exact mechanism of action may turn out to be complicated but it is a reasonable hypothesis that water, probably in both free and bound forms, is involved at some stage of the process. In that case it would be far more effective to use microwaves, rather than radiation with a frequency of a few tens of MHz. It would be well worth while investigating both the optimum frequency and the mechanism of action of electromagnetic waves when used for the treatment of malignant disease by hyperthermia.

Another phenomenon of great importance in the absorption of microwaves by biological tissue is that of resonance absorption. If it exists it could have significant repercussions as regards microwave radiation hazards. In resonance absorption a sharp peak in the attenuation coefficient occurs over a small frequency range and the presence of this peak would be unobservable outside the range. I am not aware that resonance absorption has been observed in biologic material but evidence has been advanced by Roberts and Cook (20) and by Buchanan (4) for its existence near 6 GHz in some liquid methyl esters. In view of the connection between energy absorbed and attenuation coefficient it would be satisfying to be able to preclude the existence of resonance absorption in biologic tissue over the microwave range of frequencies.

The conclusions and suggestions for future work may be summarized as follows:

(a) Although the overal dielectric behavior of biologic material at microwave frequencies is mainly determined by its aqueous content the effect of the bound water must be considered when evaluating thermal damage to the biologic macromolecules present. In general the dielectric parameters of bound water at microwave frequencies will be different from those of free water and the attenuation coefficient of the former may be higher than the latter at some frequencies. Owing to the association between energy absorption and attenuation coefficient, and to the close proximity of bound water to proteins and other macromolecules, the effect of the bound water may be crucial as regards microwave radiation hazards.

(b) In addition to their heating effect in tissues microwaves interact with the electric dipole moment of biologic molecules. These interactions may be observed and interpreted in terms of the shape and size of the macromolecules and the nature of the structure of the water in the neighboring environment. Such parameters may be correlated with the incidence and treatment of certain diseases with which the molecules in question are associated. In this way it would be possible to find a direct link between a clinical condition and a structural abnormality at a molecular level as, for example, has been done in the case of sickle-cell anemia and hemoglobin.

(c) Information about the parameters referred to in (a) and (b) can be obtained by determining the complex permittivity of the appropriate biologic material over a wide frequency and temperature range.

ACKNOWLEDGMENTS

Thanks are due to Professor R. E. Burge for providing research facilities in the Physics Department at Queen Elizabeth College. Acknowledgment is also due to the many colleagues who have participated in this work, and in particular to Dr R. J. Sheppard and Dr G. P. South.

Much of the research carried out has been supported by various grant-giving authorities and it gives pleasure to acknowledge the Science Research Council, the Wellcome Trust and the Cancer Research Campaign in this respect. Finally I would like to thank Mrs. K. M. Grant for secretarial assistance.

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SUMMARIES OF DISCUSSIONS, SESSION REPORTS AND RECOMMENDATIONS

SESSION A. GENERAL EFFECTS OF MICROWAVE RADIATION

Z. V. Gordon, T. V. Kalada. M. L. Shore and H. P. Schwan

Following Dr. Michaelson's paper a question was raised relative to the problem of extrapolation of experimental results to man. The author indicated in his reply that in attempting to make such extrapolations it is important to take into consideration all of the known attributes, similarities and differences between animals in order to develop extrapolation factors. Possibly the basal metabolic rate could be used as one of these. The question of comparability of results obtained on different animal species recurred later in the general discussion. It was felt that a sort of sliding scale based on physical (exposure conditions, the geometry of the animal relative to wavelength etc) and physiologic species specific factors is needed.

Dr. Baillie was asked about absorbed power in the rats used in his study. In response he provided the following data: average weight 216 g, temperature rise 20°C, time 60 s, specific heat 0.83. Accordingly, the rate of energy dissipation was 0.25 kW or approximately 1160 W/kg.

The presentation by Dr. Gordon raised several questions: whether the described effects on erythrocytes are characterized by threshold values; can such effects be ascribed to thermal effects; and furthermore had physical or physico-mechanical models or concepts been developed to describe the interation between microwaves and cell membranes? It was made clear during the discussion that no threshold values could be determined as no systematic quantitative study at various intensity levels had been made; further experiments are needed to obtain an answer. However, at the levels used, thermal effects are improbable and it would be difficult to conceive thermal hemolysis under such conditions. Concerning the question of physical models or concepts, Dr. Schwan indicated that two possibilities exist: either weak effects can be explained on the basis of current concepts and existing data, or the very exciting possibility exists that entirely new principles of interaction are indicated that we have not yet been able to recognize.

In response to a question about the influence of modulation patterns of microwave fields on hypothalamic and other nervous system effects, Dr. Gordon indicated that the problem of modulation had not been investigated; it may, however, play a role.

Following Dr. Servantie's presentation there was a discussion of the possibility that drugs might modify the response of experimental animals to microwaves. Dr. Servantie noted that while this might be possible, in his experiments animals were irradiated before drugs were administered. Thus he did not feel that drug modification of microwave effects was a factor in his experiments.

Dr. Mikołajczyk pointed out the necessity for careful control of seasonal and diurnal variations in any type of endocrinologic experiment. Additional discussion followed a question on dose response. It was pointed out that the pituitary gland has an enormous reserve, perhaps amounting to 85 percent. Thus when endocrine shifts are noted it is difficult to tell whether they constitute a pathologic response. No possibility exists on the basis of the results of this investigation to establish dose-response relationships, in view of the endocrine reserve and the difficulty of defining pathologic changes.

Following the presentation by Dr. Nikonova a question was asked regarding other reports from the Soviet Union on effects of microwaves at low levels. Is it possible, that the effects attributed to microwaves could have resulted from exposure to X-rays or from a synergistic or additive effect of the two radiations rather than from exposure to microwaves alone? Dr. Nikonova indicated that while X-rays and microwaves do coexist in some occupational situations, when one speaks of low intensities both of microwaves and X-rays synergism is of little significance to the observed effect. Moreover the exposure to X-rays in the USSR is carefully controlled and at least in man in industrial conditions any effects of X-ray exposure seem highly improbable.

Following Dr. Czerski's presentation a suggestion was made that the effects he had observed were those that could be expected from thermal stress on cells induced by microwaves. In response, the author noted that the power densities used in this study were not associated with significant increases in body temperature. Dr. Schwan additionally indicated that the power levels employed by the investigator were too low to produce the effects observed on a thermal basis. He pointed out that levels at least 10 times greater than those used by Dr. Czerski would have to be employed to produce thermal stresses of the magnitude needed to produce the disturbances described in the paper. The author further noted that it would be difficult to explain experimental differences between pulsed and continuous wave exposure at the same average power density on a thermal basis.

Dr. Yagi was asked.if he had observed superficial tissue burns, but replied that he had not. It was pointed out that this study was one that clearly involved significant heat stresses produced by high levels of microwave exposure.

After Dr. Rugh had concluded his presentation Dr. Gordon pointed out that Soviet investigators have observed similar effects to those observed by Dr. Rugh with 2—4 hour exposures daily during the entire period of gestation at levels of 6.5 mW/cm^2. Dr. Rugh pointed out that his study, using single acute exposures, measured integral absorbed dose. While the exact equivalence to plane wave fields was not possible, it was likely that the exposures in his study could have been higher than the dose indicated by Dr. Gordon by a factor of perhaps 15—20. This underlines the importance of studies on the effects of chronic exposures at low power intensities.

During the general discussion Drs Gordon and Schwan presented a proposal to distinguish three energy density flux levels of microwave fields. They suggested that microwave intensities be divided into the following three ranges:

(a) High intensities at which distinct thermal effects occur; in many instances such effects may be hazardous. These intensities range from 10 mW/cm^2 upwards (region of thermal effects).

(b) The range of subtle effects from about 1—20 mW/cm^2. In this range in part weak thermal but noticeable effects exist; direct field effects, as for example the phenomena of hearing pulsed fields; and perhaps, a group of other effects of a microscopic or macroscopic nature, details of which are at present unclearified (region of subtle effects or intermediate region).

(c) The region at intensities below 1 mW/cm^2. In this region thermal effects are improbable (region of nonthermal effects).

The boundaries indicated for these ranges are approximate and probably depend on numerous variable factors, such as animal size, threshold of warmth sensation, frequency, pulsing etc. The introduction of the intermediate range of subtle effects calls attention to the need for additional research, aimed at clarification of the underlying mechanisms.

The proposal to divide microwave intensities into the above three ranges was supported by several speakers. A somewhat similar proposal was made previously at the symposium of the New York Academy of Sciences, held in New York in September 1972, on "Electrically mediated growth mechanisms of living systems". The three levels were termed non-thermal (1 μW — 100 μW); thermal, non-heating (100 μW — 10 mW) and heating (over 10 mW).

It was stressed that such limits are very relative and only further studies may make it possible to outline such limits more precisely. It was also stressed that relative species sensitivity should be considered in outlining such limits. A sort of sliding scale for species may be needed. It would be also most desirable to add one more parameter to the description of experimental conditions in microwave research, namely the absorbed dose expressed in appropriate terms to insure uniformity in published research. Significant discussion of this proposal took place among the participants with general support being given to it.

The widespread use of microwave power for industrial, civilian, and military purpose has greatly increased the possibility of exposure of large population in many countries of the world. Protection of exposed populations by means of health and safety standards has varied widely in different parts of the world, in largo measure because of differences in scientific theory and method.

Several papers (e.g. that of Dr. Michaelson) were devoted to the biologic effects of higher intensities. The majority of papers concerned the biologic effects of low intensities (e.g. that of Dr. Gordon and her collaborators). These intensities are so low that distinct thermal effects can be excluded. However, in a few of these investigations, the possibility exists that microthermal effects and nonthermal effects which are unclear at the present time might have occurred. These phenomena may be responsible for the biologic changes observed.

These investigations have been concerned with microwave effects in complex biologic systems. The use of medical methods of approach and the end results of the influence of microwaves were correlated with field intensities. These investigations did not permit explanation of the mechanism of microwave interaction with biosystems.

In addition to the general recommendations that are given at the end of the Proceedings (see p 334), the following specific conclusions and recommendations were agreed upon:

1. The majority of the investigations carried out at present use medical approaches. In this approach the microwave stimulus of interest is applied to the biologic system and the end result of clinical or biologic interest is registered. Biophysical investigations are also important. They concern up to now mostly effects on isolated components (e.g. membranes, molecules). A fairly advanced understanding has been achieved even though many problems remain unsolved. Only very few data exist on biophysical mechanism of microwave interaction with complex microscopic and submicroscopic systems (e.g. intermolecular mechanisms). This situation should be remedied. More biophysical investigations are needed before clarification and understanding of the subtle effects will be possible. Special attention should also be paid to investigations to determine the absorbed energy dose and its spatial distribution.

2. Investigations of the effects of low microwave intensities should be developed with the aim of determining threshold values at which biologic effects are induced. An evaluation should be made of the significance of subtle effects for biologic function. Combined effects of microwave and of other environmental factors should be investigated. Particular attention should be paid to investigations of bioeffects induced at various microwave frequency bands.

3. Biologic, medical, and biophysical investigations of radiofrequency effects in the entire radiofrequency range should be carried out. Particular attention should be paid to the dependence of biologic effects on the physical characteristics of the electromagnetic field.

4. There is a need for further research to clarify and improve our understanding of the interaction of microwave and radiofrequency radiation with biologic systems at all levels of organization to provide and improve understanding of the full potential for: (a) cumulative effects, (b) delayed effects, (c) differential radiation sensitivity (i.e. sensitivity as a function of type of the system and the stage of development), (d) effects related to cellular transformations, (e) carefully controlled human epidemiologic studies.

SESSION B. INFLUENCE OF MICROWAVE RADIATION ON THE NERVOUS SYSTEM AND BEHAVIOR

W. R. Adey, E. A. Lobanová, A. V. Roščin and W. A. G. Voss

Papers presented in this session emphasize difficulties inherent in evaluating subtle physiological and behavioral effects in mammals during and following microwave exposure. In part, these uncertainties relate to intercurrent stimuli, sometimes unsuspected during field exposures. They may elicit autonomic nervous reactions in the organism closely resembling field-induced changes. Moreover, long-continued, low-level exposures must take account, for example, of such natural factors as growth and aging, with consequent changes in endocrinologic status, before a causal role can be assigned to effects of microwave exposure. As with ionizing radiation, there are perplexing questions about cumulative effects and dose division. There are special problems in electrophysiological recording in the CNS during microwave exposure, since inappropriate metal recording electrodes may be associated with excessive energy absorption, and thus, with tissue heating and lasting damage. These concerns were explicit in the papers presented in Session B and in the ensuing discussion.

In her use of conditioning methods, Lobanova noted many changes in operant conditioned responses in rabbits irradiated for 1 hour daily in a field of 10 mW/cm^2 for 4 months, but not until the fourth month of exposure. Return to normal responses occurred only two months after irradiation. She reported that rats irradiated for 6 months became apathetic, often not responding, and failed to react to the quality of food. These findings typify the difficulty of quantitatively measuring such subtle effects, reminiscent of many similar reports by Soviet workers of effects of low-level exposures in man. Lobanova ascribed these effects to altered cortico-subcortical relations involving the hypothalamus, hippocampus and sensorimotor cortex, with a slow cortical EEG coinciding with convulsive hippocampal activity. Baranski and Edelwejn also implicated subcortical sites, and particularly the reticular formation, in their EEG and evoked potential records, which combined pharmacologic manipulation by phenactin, cardiazole and pentobarbital with chronic daily microwave exposure.

Findings by Goldstein and Sisko of an intense behavioral arousal in rabbits following brief irradiation at 9.1 GHz, with a response latency of 3 to 12 minutes, may be more difficult to interpret since the effects disappeared when the environmental humidity exceeded 40 percent. Could this be a peripheral effect on skin or fur, or is it mediated by some slowly activated central nervous humoral mechanism? If central, could the microwave field in central nervous tissue be enhanced by the presence of metal electrodes? The question of thresholds for thermal effects within the crania of test animals, with and without potential distortions of the EM field that might follow implantation of inappropriate metal electrodes, was repeatedly raised in discussion of these papers. It was pointed out that absorbed powers in the head of a rabbit could be in the range of 14 to 40 W/kg for exposure levels of 7 to 20 mW/cm^2, and that this might be 3 to 10 times above the threshold for thermally induced CNS effects.

The high general level of interest in the problems of instrumentation in studies of the central nervous system led to a separate informal session. It was agreed that recording of temperature during or immediately following irradiation of the brain would be of great importance. Several viewpoints were expressed on possible solutions to the problems of electrodes for bioelectric recording during exposure. It was suggested that saline filled glass electrodes with a metal ball at the tip might be feasible. Alternatively, wire electrodes, insulated with a high-quality dielectric, short with respect to the wavelength of the field and having a broad surface at the electrode tissue interface, might be suitable. Further research on electrode and electrode-amplifying systems was recommended.

To obviate the need for recording directly in the CNS, while retaining a useful measure of stress responses during microwave exposure, Justesen has used an "evoked colonic temperature". He noted that simply handling rats raised body temperature, and that this initial rise with handling was enhanced by microwave exposure. He interpreted these findings in terms of a Pavlovian orienting reflex to novel stimuli. This view was not accepted by Soviet participants, who emphasized the ephemeral character of an orienting response following the initial reaction to novelty.

In studying the effects of pulsed fields on animals with audiogenic epilepsy, Štverak, Marha and Pavkova emphasized the significance of the envelope of the carrier wave in seizure induction. This question of the significance of modulation envelopes in determining biologic sensitivity to the field has received very little attention, although recent studies by Bawin, Medici and Adey of low level UHF fields, amplitude modulated at 2 to 20 Hz, have shown their potency in modifying conditioned reflexes and EEG rhythms.

Romero-Sierra reported effects of 16 GHz fields at 25 mW/cm^2 on birds. These included altered EEG and EMG records, with increased high frequency activity. His findings also implicate the modulation pattern of the microwave carrier. These studies in behavioral neurophysiology were accompanied by evidence of concomitant structural changes in neuroglial-neuronal interrelations. Much further work is suggested by these proposed schemes of tissue interaction with microwave fields. They quite appropriately draw attention to recent developments in membrane structure, including the model of the "greater membrane", as proposed by Schmidt and Samson. The surface layers of glycoprotein that characterize the greater membrane may well be the site of threshold interactions with modulated microwave fields, in view of their strongly polyanionic character and capacity to reversibly bind water and divalent cations, particularly calcium. There is now much evidence that the initial events in excitation of the neural membrane may involve calcium in small shifts between closely adjoining binding sites on sheets of membrane surface macromolecules. Such a mechanism may underlie these interactions with weak electromagnetic fields.

Dr. Romero-Sierra mentioned certain possibilities of beneficial effects of microwaves. In this connection the work of Mr. Priore from Bordeaux was mentioned. Many participants expressed their interest in this work. Dr. Servantie very kindly supplied a list of references.*

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* References: 1. Berteaud, A. J., Bottreau, A. M., Priore, A., Pautrizel, A. N., Berlureau, F., Pautrizel, R.: *C. R. Acad. Sci. Paris,* 272, 1003, 1971. 2. Delmon, G., Biraben, J.: *Rev. Path. Comp.,* 1966, 3, 85. 3. Mayer, G., Priore, A., Mayer, G., Pautrizel R.: *C. R. Acad. Sci., Paris,* 1972, 274, 3011. 4. Pautrizel, R., Riviere, M., Priore, A., Berlureau, F.: *C. R. Acad. Sci. Paris,* 263, 579, 1966. 5. Pautrizel, R., Priore, A., Berlureau, F., Pautrizel, A. N.: *C. R. Acad. Sci. Paris,* 268, 1889, 1969. 6. Pautrizel, R., Priore, A., Berlureau, F., Pautrizel, A. R.: *C. R. Acad. Sci. Paris,* 271, 877, 1970. 7. Pautrizel, R., Priore, A., Dallochio, M., Crockett, R.: *C. R. Acad. Sci. Paris,* 174, 488, 1972. 8. Rivière, M., Priore, A., Berlureau, F., Fournier, M., Guérin, M.: *C. R. Acad. Sci. Paris,* 259, 4895, 1964. 9. Rivière, M., Priore, A., Berlureau, F., Fournier, M., Guérin, M.: *C. R. Acad. Sci. Paris,* 260, 2099, 1965. 10. Rivière, M., Priore, A., Berlureau, F., Fournier, M., Guèrin, M.: *C. R. Acad. Sci. Paris,* 260, 2639, 1965. 11. Rivière, M., Guérin, M.: *C. R. Acad. Sci. Paris,* 262, 2669, 1966.

The reaction of the central nervous system to microwaves may serve as an early indicator of disturbances in regulatory functions of many systems. The extraordinary sensitivity of the nervous system to microwaves was clearly demonstrated by the findings presented in all the 6 papers, concerning this topic.

The investigations on the conditioned reflex function, behavior and differential reactivity of particular brain structures to microwaves are very important for the understanding of symptoms observed in personnel occupationally exposed to microwaves.

The data presented during this and other sessions are of great importance for the setting up of safe exposure limits, one of the basic problems in preventing untoward effects on the health of occupationally exposed persons.

The session recommended that further investigations on microwave effects in the nervous system should include:

1. Investigations on the influence of microwave exposure on behavior and conditioned reflex function using various exposure regimes. The results hitherto obtained indicate that such effects may depend on the exposure regime, but it should be stressed that possible relationships are insufficiently known.
2. Electrophysiologic investigations seem to be of particular interest. Such investigations carried out during the exposure period are particularly needed. Unified, standard electrodes permitting recording during exposure without interference from the microwave field should be developed. This is a task for an international cooperative effort. The results obtained by Dr. Guy indicate the need for such electrodes.
3. It is to be regretted that no data on the effects on central nervous system metabolism were presented during the symposium. Investigations, without which nothing can be said about the mechanism of the disturbances of regulatory functions of the central nervous system, are urgently needed.
4. A lack of data on morphologic changes in the central nervous system was also felt. Investigation on microwave effects of the electron microscopic, cytochemical and histologic picture of the brain should be carried out.

SESSION C. EFFECTS OF MICROWAVE RADIATION AT THE CELLULAR AND MOLECULAR LEVEL

E. H. Grant, K. H. Illinger, B. Servantie and S. Szmigielski

Discussion of Dr. Schwan's paper was devoted to a number of fundamental points. The size dependence of the pearl-chain effect, with the voltages required to achieve alignment of macromolecules, cells and particles of 100 micron size, was discussed.

In principle, a wide range of particles may exhibit pearl-chain formation, but with threshold voltages critically dependent on particle size. For macromolecules voltages in excess of 10 $kVcm^{-1}$ are required; for cells and particles of 100 micron size, threshold voltages are of the order of 100 Vcm^{-1} and 1 Vcm^{-1}, respectively. The fact that the order of magnitude of the threshold for microwave hearing shows a dependence related to the pearl-chain effect was pointed out; the threshold is given by the expression: (400 mW/cm^2) (duty cycle)$^{-1}$. Fundamental to predictions concerning the dielectric behavior of membranes is the accuracy of the model employed. It was stressed that the currently accepted model, the Hodgkin-Huxley model, is consistent with the following behavior; requisite for the excitation of membranes by external EM fields are two conditions: a) the field strength must exceed the membrane firing potential, and b) the period of the field must equal or exceed the refractory period of the membrane. If any inadequacies exist in the Hodgkin-Huxley model, these criteria might not apply; in particular, other models for the nature of extracellular fluids may predict effects on membrane excitation through intermolecular rearrangement. The fact that dielectric saturation of biopolymers requires very large field strengths, of the order of 10 $kVcm^{-1}$, was adduced to explain the vanishing likelihood of protein denaturation by EM fields at low field strengths. The dynamic potential which exists in certain membranes, superimposed upon the average (static) potential, is not included in the assessment of interactions with EM fields, but the accumulation of energy in a membrane via external fields is inconsistent with the Hodgkin-Huxley model. As a general comment on the predictiveness of existing theoretical models, it was pointed out that there exists the possibility that effects at the level of biologic systems may not be predictable on the basis of the behavior of isolated molecular systems.

The question of the energy difference between conformational states of biopolymers was raised. As a general result, it was stressed that resonant interactions between EM radiation and molecules of biological interest are the more improbable the lower the frequency of the EM field; conversely, resonant interactions in molecular systems become paramount in the limit of high frequencies. Molecular collisions are strongly diabatic with respect to rotational and translation states, and strongly adiabatic with respect to electronic and vibrational states. Hence, EM radiation interactions are of the relaxation type at frequencies below 1 cm^{-1}, of the resonance type at frequencies above 100 cm^{-1}, and of an intermediate nature in the far-infrared region. As a result, EM fields in the microwave and RF region, below dielectric saturation levels, are unlikely to cause irreversible effects at ordinary *in vivo* temperatures.

Regarding the studies of microwave irradiation of biologic preparations represented by several papers, the effect of the shape and nature of the sample container, and of the depth of liquid, on the actual field in the sample was stressed repeatedly. Sample containers and the liquid in which the sample is suspended may act as dielectric lenses and/or reflectors and cause localized hot spots in the sample, which may render dosimetry inaccurate.

The question of the existence of cumulative effects in cataractogenesis by microwaves was discussed at some length. Michaelson argued for the re-examination of the concept of cumulative effects. It was also pointed out that latency times for cataractogenesis differ greatly from animal to man, and that the interrelation between injury and repair in the body renders a definition of a cumulative effect difficult. It was also stressed that errors of up to ±70% in the dosimetry can occur due to the characteristics of the body of the subject being investigated.

Dr. Baillie defended the concept of "cumulative effects" of microwave radiation from the medical point of view on a theoretical basis. If microwaves produce injury in tissue one cannot assume that the change is eliminated when the power is turned off. The return to normal (if a return to normal is possible) takes time. Accordingly and by definition, repeated exposure to microwaves may produce cumulative injury (whether functional, biochemical or structural) provided that the exposures are made with sufficient frequency. A progressive injury passing from functional through biochemical to structural forms is completely reasonable.

This standpoint was supported by Dr. Shore, who stated that while the question of cumulative effects was not a central theme of his presentation, Dr. Carpenter has obtained data demonstrating that single doses of microwave radiation which do not produce cataracts, become cataractogenic when they are administered daily for 15 consecutive days. He interpreted these data as providing evidence for a cummulative effect. Careful attention must be also paid to studies demonstrating that fetal effects which have been observed following relatively high acute exposures (Rugh) are also observed when animals are exposed to much lower levels of microwaves, but under conditions of chronic exposure (Gordon). These studies as well as the studies of EEG effects provide presumptive evidence for cumulative effects. This is, however, an important question that requires further discussion and research.

In connection with Dr. Stodolnik-Badańska's paper, it was proposed that the study be complemented by using Caspersen's technique for chromatids.

The problem of avoiding runaway heating in the microwave heating of frozen tissue was discussed in connection with Dr. Voss's paper; the essential role of cryoprotective agents and other means to avoid this difficulty was pointed out. The structure and dielectric properties of water in cryogenically cooled tissue were discussed.

The principal conclusions drawn from each of the six papers presented are as follows:

1. Biologic tissue exhibits three main dispersions:

(a) alpha-dispersion due to countersion movement about the charged cell surface and relaxation of the membrane properties.

(b) beta-dispersion due mainly to the membrane reactance but also partly to relaxation of monomolecules.

(c) gamma-dispersion due to free water; a small delta-dispersion exists between the beta and gamma dispersions due to bound water and to side-chain relaxation.

Analysis of electromechanical forces involved in biologic systems subjected to pulsed radiowaves and microwaves shows that the threshold for hearing effects in the middle ear is 400 mW/cm^2 divided by the square root of the duty cycle.

2. Resonance absorption phenomena are theoretically possible in biopolymers at around 30 GHz and are therefore a possibility in biologic tissue if the water content is low. Any such selective absorption of energy over a narrow frequency band would have important implications for the evaluation of microwave hazards.

3. If washed rabbit erythrocytes are exposed to 3 GHz microwaves at a level of 1 mW/cm^2 the following efflux of substances is observed:

(a) the potassium after 15—30 minutes;

(b) the hemoglobin after 120—180 minutes.

With granulocytes the effect of the microwaves is to cause the appearance in the supernatant of acid phophatase and lysozyme. This occurs after 120 minutes of irradiation, also at 1 mW/cm^2 intensity.

4. In any experiments involving the effect of microwaves on animals, the importance of measuring power density properly should be stressed. In experiments carried out on the rabbit eye variation of such parameters as the animal's shape, size and ear position can affect the measured power density at the eye as much as 70%. The importance of well defined and well controlled experimental conditions is therefore quite clear.

Soon after the exposure of the lens to microwaves inhibition of DNA synthesis in the lens epithelium is noticed and decrease in ascorbic acid concentration observed. This happens before the opacities develop. It is therefore suggested that the microwaves interefere with lens metabolism.

5. The influence of microwaves radiation on human lymphocytes may be studied:

(a) when the lymphocytes are unstimulated,

(b) when the lymphocytes are stimulated to mitosis by PHA treatment.

In the former case the lymphocytes were transformed to blastoid forms and macrophage-like cells. In the second case mitotic anomalies were observed and were characterized by the occurrence of abnormal chromosomes and bridges between the chromatids and chromatid breaks.

6. Microwaves are a very effective way of re-warming deep-frozen organs and cells.

The method has been used with adult canine kidneys, fetal mouse hearts and tissue culture cells.

With the fetal mouse hearts recovered from — 196° by microwave heating, the electrical activity has survived in the majority of cases, and tissue culture cells have been found to withstand a very rapid rate of thawing.

Summing up this session, the following recommendation is made:

Work of the kind described in this session should be encouraged and further extended. To obtain reliable results, however, a multidisciplinary approach is essential. Such investigations should be tackled by a team of investigators comprising at least one of each of the following: doctor, biophysicist or physicist, and electrical engineer. Such a team may not necessarily be all located in one establishment: this may be too expensive to arrange on a wide scale. In this case inter-department collaboration is a satisfactory substitute provided all participants meet regularly.

SESSION D. MEASUREMENTS OF MICROWAVE RADIATION

R. C. Baird, P. Czerski, A. W. Guy and M. Piotrowski

A clear understanding of the biologic effects observed in man, animals and biologic specimens exposed to electromagnetic fields requires a complete quantitative description of the fields both inside and outside the test subject. These fields are complex functions of the types of sources and the shape and size of the exposed subject or sample. If these effects are ignored estimates of absorbed power can be in error by several orders of magnitude. Above 200 MHz the combination of curved surfaces and high dielectric constant of tissues can produce very high localized internal absorption deep in the tissue due to focusing of the field. Below 200 MHz the absorbed power in exposed subjects drops sharply with frequency. In this range the unperturbed magnetic fields can produce far greater absorbed power densities in man than unperturbed electric fields of the same energy density, whereas the reverse is true in small animals. Internally placed metal or highly conducting probes can produce intense localized absorption due to the fringing of fields near sharp edges or points.

The external fields have usually been specified in terms of power density, but it was pointed out that this quantity is not always a good indication of the hazardous potential of a field. Further, existing instrumentation actually responds to the electric field or the square of the electric field, both of which are more reliable indicators of the possible biologic effects (except at the lower frequencies where magnetic fields may become more important). Three different types of meter were described.

The first, consisting of two thin-walled coated spheres connected by a small tube, is essentially a spherical bolometer and absorbs radiation in a manner similar to the human body. It responds to the average absorbed power and has been operated from 400 MHz to 35 GHz. This instrument is not manufactured commercially, but it may be worthy of further consideration. The second type of meter employs three orthogonal dipole-diode combinations to form an isotropic sensor that measures either the square of the electric field or each of the individual components of the field.

The advantages of this sensor are that it can be made very small (less than one cm in diameter), it is rugged and has a dynamic range in excess of 40 dB (a factor of 10^4). Models capable of being implanted seem possible. Peak power reading versions can also be constructed. The third type of meter uses an orthogonal assembly of thermocouples and also reads only the average power. It is incapable of reading peak power, but will function properly in a multifrequency field.

The necessity of accurate instrument calibration was emphasized. Such calibrations are essential for safety reasons and to provide a reliable basis for comparison of the experimental results of various laboratories. Three basic approaches to the calibration problem were discussed — the free-space standard field method, guided wave methods, and the standard probe or transfer standard method. All of these methods can be used for reasonably accurate calibrations if sufficient care is taken, but one must be aware of several problems in each method. Calibration accuracies of about 3 to 10 percent can be achieved, depending on the method used and the instrument being calibrated. However, one cannot expect such accuracy when using the meters for actual measurements because (a) meters are usually calibrated in plane-wave fields and such fields are seldom encountered in practice, (b) in most calibration methods only the sensor is exposed to the field while in practice the entire instrument, including interconnecting cables, is immersed in the field, and (c) with hand-held meters, the presence of the operator will perturb the field and affect the reading. These uncertainties are difficult to assess, but an attempt should be made in each situation.

Internal fields and power absorption may be directly measured *in vivo* by implanted electromagnetically transparent probes, although accurate and reliable implantable probes still need to be developed. Internal power absorption can also be measured using thermographic techniques on phantom models or sacrificed animals. This is done by thermographically observing related temperature changes in bisected sections of the model or animal after a short exposure to an electromagnetic field.

In connection with internal fields and power absorption the problem of perielectrode energy absorption in brain tissue was discussed at some length. Dr. Guy was of the opinion that the energy concentration and the resulting thermal gradient at the tip of the electrode is a function of the impedance of the leads and amplifier as well as of the electrode-tissue interface impedance. Though simple impedance considerations may be used to quantify the thermal gradient for quasi-steady conditions, the complexity of the model for microwave exposure requires a rigorous solution of the EM equations for antenna buried in lossy media (see for example the special IEEE PGAP, *Transactions on antennas buried in lossy media* published about May, 1962). In general any time a sharp metal object is put in contact with tissue, field enhancement will result at the point of contact.

The thermograph presented in Dr. Guy's study used an electrode described by A. H. Frey, in "Brain stem evoked responses associated with low intensity pulsed UHF energy". *J. Appl. Physiol.*, vol. 23, pp. 984—988, Dec. 1961. The electrode was connected to a lead several feet long. The electrode was placed 2 to 3 cm deep or approximately one half wavelength or more into the medium.

At microwave frequencies with wavelengths of the order of centimeter in tissues it may be difficult to isolate insulated electrodes in this manner. Certainly some studies should be carried out to see to what extent the enhanced fields may be treated as a function of electrode properties.

Interference or diffraction patterns produced when a human subject is exposed to a microwave field of 1 to 3 GHz were described. These studies show that the field is strongly perturbed by the subject. Consequently, in experiments involving more than a single animal one must be careful to space the animals sufficiently far apart so that one animal does not perturb the field in the region of another animal. These results also illustrate the effect that an operator can have on the field he is trying to measure when using a hand-held probe. This is one factor which is hindering the development of a reliable personal dosimeter. Reflection and transmission measurements of this type will also allow a new approach to the estimation of absorbed energy in different parts of the human body.

A simplified method of determining the radiation hazards associated with moving radar antennas was described. The method avoids the tedious measurement procedures used previously by employing assumed radiation patterns which are based on selective measurments. These assumed patterns are used to calculate the field intensities at points of interest. The method was applied to rotating and scanning antennas, and is applicable to the evaluation of situations involving several radiating sources operating at the same time.

There is a need for complete data on the dielectric properties of biologic substances, and a method for determining the dielectric constant of samples placed within a cavity resonator was presented. The theoretical approach and the experimental apparatus were described. Both the real and imaginary parts of the dielectric constant were obtained from measured values of the resonant frequency and the Q (quality factor) of the cavity. Measurements of various samples were carried out at the X-band.

The following recommendations were approved by the participants involved in microwave measurements:

1. Accurate, internal dosimeters are needed for biologic research. Efforts should be increased to quantify internal fields in future work.
2. Standard methods of quantifying internal and external fields and detecting the biologic signals should be established.
3. Standardized exposure techniques for animals and *in vitro* samples would significantly improve our ability to compare results between different laboratories.
4. Researchers should describe all pertinent experimental conditions, including the size and shape of test samples, etc.
5. The development of magnetic field sensors should be promoted in view of recent indications of strong interaction with the magnetic fields at frequencies below about 200 MHz.
6. More complete information on the electromagnetic and thermodynamic properties of biological materials are needed. The development of techniques for measuring these properties in a non-destructive manner on living organisms would be extremely useful.
7. An interdisciplinary group should be established to translate and disseminate documents pertaining to both the biologic and engineering (physics) aspects of research on the biologic effects of electromagnetic radiation.

SESSION E. OCCUPATIONAL EXPOSURE AND PUBLIC HEALTH ASPECTS OF MICROWAVE RADIATION

Z. Edelwejn, R. L. Elder, E. Klimková-Deutschová and B. Tengroth

The difficulties of rigidly controlled clinical and epidemiologic studies were discussed, particulary in long-term studies. Since at present no reliable methods and equipment for individual dosimetry exist, the exposure of microwave workers must be estimated on the basis of measurements made at working places and mean daily (weekly, monthly) duration of exposure. In many instances this may be difficult, as for example in cases where the individuals exposed move about and work with moving microwave beams. The type of work should be taken into account. Depending on the type of work, exposure to near or far fields may predominate, which influences the reliability of dosimetric data. Possibilities of incidental or accidental (high level) exposures must also be estimated.

Particular attention should be paid to possible effects of other environmental factors which may occur at working places where microwave equipment is used. Two factors were mentioned specially during the discussion: ambient temperature (microwave welding) and exposure to X-rays, generated incidentally by many parts of microwave apparatus.

Dr. Sadčikova stressed that all these considerations were taken into account in the studies that she had described. In particular the ambient temperature was not elevated and X-ray exposure was controlled. It may be stated that the microwave workers examined in her studies were not exposed to incidental X-rays. It should, however, be stressed that the persons examined began their work before the present USSR safe exposure limits were introduced. Because of this the "occupational case history" includes periods of exposure which were higher than allowed by the present USSR regulations.

During the discussion it was also stressed that no serious cardiovascular disturbances were ever seen in man (or in experimental animals) as the result of microwave exposure.

According to the authors and discussants, most of the significant clinical findings (subjective complaints, physical examination, bioelectric recordings) in the case of microwave long-term exposure or overexposure are referable to the nervous system. The term "microwave neurosis" was mentioned.

A lively, but inconclusive discussion concerned microwave lens injury. According to Dr. Zaret microwave cataracts are characterized by typical traits, seen on ophthalmologic examination and easily recognizable. According to Dr. Żydecki long-term microwave exposure may cause an "acceleration" of the normal aging process, and more opacities and discrete lens changes are to be seen in microwave workers than in comparable age groups. No characteristic morphologic traits are, however, to be found. Dr. Appleten confirmed his results published earlier *(Arch. Ophthalmology,* 88, 259, 1972) that no differences in lens translucency between microwave workers and comparable age groups of unexposed persons can be found. These results are additionally confirmed now by examination of about 1500 military personnel working with microwave equipment. No explanation of these differences could be found. Particular attention should be paid to retinal lesions in microwave workers, the general impression being that such lesions could have been overlooked in earlier studies.

In the papers on microwave eye damage the problem of cataracts seems to dominate. Whether the cataracts observed are of a special type or not, cannot be clearly defined. There seems to be convincing evidence that opacities in the lens occur among microwave workers. It is suggested but not proven that this is a result of exposure to microwaves. In most microwave workers investigated, where opacities have been demonstrated, these changes have no clinical significance. However they may be of great importance as they may be signs of a developing cataract. Retinal changes have been reported. In order to understand these eye changes further epidemiologic studies should be carried out in combination with theoretical and experimental work. There seems to be no evidence that these changes are anything but thermal in origin.

The above discussion led to a consideration of the problem of adequate control groups. No satisfactory solution could be offered. It is extremely difficult to find human groups differing only in one variable — degree of microwave exposure or exposed and unexposed groups indentical in other respects. All medical epidemiologic studies involve similar questions and doubts, requiring final experimental verification.

The specificity of the clinical symptoms of microwave effects was illustrated in several groups of occupational exposure according to the clinical picture. Autonomic disorders and cardiovascular and hemodynamic functional disturbances were emphasized. The neurologic picture may indicate the possible hazards in the working environment. Computer analysis of large groups according to various types of exposure and clinical symptoms, electrophysiologic and biochemical results make it possible to obtain information on the quality, main stages of involvement and localization of lesions in the nervous system. The problems of the mechanisms operative in disturbances of the nervous system may be explained by the rectangular branching of vessels leading to the brain stem and to the temporal region, with slowing of the blood flow and decreased oxygenation. A thermal effect can be assumed to be responsible for the symptomatology of the fossa posterior. Methodological aspects of examination were emphasized. Preventive measures may be deduced from clinical results and criteria can be established for persons to be excluded from work with microwaves.

Attention has been paid to biochemical changes, such as glucose tolerance, pyruvic and lactic acid levels as well as of creatinine in the urine, blood protein with precise correlations to the working conditions, the levels of cholesterol, 17-ketosteroids, etc. In most cases biochemical changes may be attributed to changes of regulative mechanisms.

A very lively discussion was concentrated on thermal effects and unspecific influences in working conditions and on the problem of biologic effects and health aspects in the population, where the hazards of microwave and ultra-high-frequency electromagnetic fields may play a role in living conditions.

On the basis of the clinical studies presented the following recommendations were made:

1. To seek further suitable preventive measures not only for persons exposed to microwaves at work but also for the general population in possible danger.
2. To make further epidemiologic comparative and dynamic studies.
3. To stress the evaluation of refined tests of motor system function as a diagnostic tool for the estimation of the exposure to microwaves.
4. To include the examination of the retina in all ophthalmologic examinations.

SESSION F. PRESENTATION AND DISCUSSION OF SESSION REPORTS, CONCLUSIONS (INCLUDING FUTURE RESEARCH NEEDS) AND RECOMMENDATIONS

J. C. Gallagher, K. V. Nikonova, E. Shalmon and C. Susskind

Only a single paper was presented during this session. Dr. Grant pointed out that microwaves can be used as tools in biological research. He described some of the recent research in his laboratory in which the dielectric constant of lipoproteins from patients with hyperbetalipoproteinemia (a condition associated with coronary heart disease) was compared with that of normal lipoproteins. Measurements on other macromolecules were also described. These experiments may serve as examples of research topics to be investigated in the future.

A discussion on bound water in tissues ensued. Eye tissue contains a substantial percentage of bound water. Dr. Oderblad, Sweden, has conducted studies by NMR (nuclear magnetic resonance) on bound water. Professor Schwan has also carried out dielectric relaxation studies on eye tissue. The determination of bound water by NMR studies does not give the same result as does dielectric relaxation, but gives an indication of it. The outer segments of the rods and cones in the retina consist of small quantities of water. The content of bound water in this region has not been studied and should be investigated. This would highlight the importance of any bound water and increase the probability of resonance absorption effects.

The second part of the session was devoted to presentation by the respective Chairmen of the session reports, conclusions and recommendations. These concerned mainly future research needs and directions. Many speakers supported the conclusions reached at particular sessions. The general feeling was that for further development of research on microwave bioeffects international collaboration and coordination of efforts under the auspices of an appropriate international agency are most important. The most significant points of the conclusions and recommendations were selected and are presented under a separate heading in this book (pp. 334—335).

EXPRESSION OF APPRECIATION

Professor A. V. Roščin, USSR, addressing the Symposium on behalf of all the participants, said: During the past four days, we have all participated intensively in the work of the first International Symposium on Biologic Effects and Health Hazards of Microwave Radiation. For us, who are specialists working toward the protection of man from the harmful effects of such radiation, the Symposium has been an event of very special and lasting importance.

The British author Bernard Shaw once said that if two friends exchange apples, each still has only one apple, but if they exchange ideas, then each has two ideas. The importance of our Symposium lies in the fact that it has provided us with an opportunity to exchange ideas and opinions about what has been done in the past and what we have to do in the future.

When I made plans to attend the Symposium, my past experience of similar meetings made me afraid that there would be a wide divergence of views because the scientific problems posed by microwave radiation are still very new; they have been a matter of concern for only a little over twenty years.

Thanks, however, to the very able and judicious organization of the Symposium, it has been possible for us to combine the many different streams of knowledge, springing from sources all over the world, into a single river flowing along a clearly determined course. This happy result will undoubtedly be highly stimulating for further work in the field of microwave research.

I would like to stress here the important role that the Polish co-sponsor played in the successful organization of the Symposium. The Poles are noted for their hospitality and talent for international collaboration and they have displayed these qualities brilliantly in the present Symposium. I feel that we all have reason to be deeply grateful to our Polish hosts, the official Polish organizations and the Polish co-workers for the contributions they have made to the success of the meeting.

I have also been greatly impressed by the goodwill of the American co-sponsor, who has played such an important part in the organization and work of the Symposium. I could go on to enumerate the many other countries that have also participated and whose representatives have brought along knowledge and shared it freely with us all. It is obvious that a vast amount of goodwill has been demonstrated by all the speakers.

Dr. R. L. Elder, USA, proposed that the participants express their thanks to the principal hosts and sponsors of the Symposium and their staff, with deep appreciation of the excellent arrangements made for the Conference, which had contributed so much to the spirit of goodwill and cooperation prevailing during the discussions. The proposal was approved unanimously.

CONCLUSIONS AND RECOMMENDATIONS

The widespread and increasing use of microwave power has greatly increased the possibility of exposure of both occupational and general population groups in many countries of the world. Protection measures and health and safety standards have varied widely in different parts of the world mainly because of differences in research approaches, findings and interpretations. In so far as possible, it is imperative to resolve or remove obstacles to a common understanding of the scientific basis for protective measures.

The accomplishments of this memorable international symposium, in terms of meaningful exchange of data, frank discussion of viewpoints, enthusiastic interest in opportunities for collaborative undertakings, and the recommendations that follow, constitute a significant step toward the advancement of knowledge in the field.

The following recommendations were made:

1. To promote international coordination of research on the biologic effects of microwave radiation there should be a continuing exchange of information, improved efficiency of translation services, exchange visits, and closer collaboration in research projects and publications.

2. A program concerned with non-ionizing radiation should be developed by an international health agency that could exert leadership in this field and facilitate communication among scientists. It was hoped that the World Health Organization would assume this responsibility.

3. Every effort should be made to establish internationally acceptable nomenclature and definitions of physical quantities and units and to standardize measurement techniques and dosimetry. An international group should be established to work out procedures for achieving these objectives.

4. To achieve a more uniform approach to the discussion of mechanisms underlying biologic effects, it is proposed that microwave intensities be considered as divided into three approximate ranges as follows:

a) The range above 10 mW/cm^2 in which distinct thermal effects predominate.

b) The range below 1 mW/cm^2 in which thermal effects are improbable.

c) An intermediate range in which weak but noticeable thermal effects occur as well as direct field effects and other effects of a microscopic or macroscopic nature, the details of which have not yet been clarified.

The limits of these ranges have not yet been determined. They may differ for various species and may also depend on a variety of parameters, such as modulation and frequency.

5. In view of the importance of electrophysiological recording for studies of microwave effects there is need for the development of new electrode systems and integrated electrodeignal amplifying systems capable of use and full operation during microwave exposure.

6. Further biologic, medical, epidemiologic and biophysical studies are needed to improve understanding of the interactions of microwave radiation with biologic systems and clarify the risks that may be associated with microwave exposure. Specific attention should be given to the following:

a) investigation into the occurrence of cumulative effects and delayed effects;

b) study of low-intensity effects;
c) determination of possible threshold values;
d) study of combined effects of radiation and other environmental factors;
e) investigation of differential radiation sensitivity as a function of organ system and age or intrauterine development;
f) study of effects related to cellular transformations;
g) study of effects occurring at the molecular level; and
h) determination of absorbed energy dose and its spatial distribution.

The desirability of conducting similar investigations in the radiofrequency range was emphasized.

LIST OF PARTICIPANTS

Dr. **W. R. Adey**	Professor, Anatomy and Physiology, Center for Health Sciences, School of Medicine, University of California, Los Angeles, California 90024, USA.
Dr. **B. Appleton**	Chief, Ophthalmology Service, Department of the Army, Walter Reed Army Medical Center, Washington, D. C. 20012, USA.
Mr. **H. D. Baillie**	Lecturer in Surgery, Department of Surgery, The Royal Infirmary, University of Manchester, Manchester M 13 9 WL, UK.
Dr. **R. C. Baird**	Chief, Electromagnetic Fields and Antennas Section, Electromagnetic Division, National Bureau of Standards, Boulder, Colorado 80302, USA.
Dr. **S. Barański**	Professor and Director, Military Institute of Aviation Medicine, ul. Krasińskiego 54, 01-755 Warsaw 86, Poland
Dr. **D. E. Beischer**	Professor and Chief, Biomedical Division, Naval Aerospace Medical Research Laboratory; Pensacola, Florida 32512, USA.
Mr. **R. R. Bowman**	Scientist, Electromagnetics Division, National Bureau of Standards, Boulder, Colorado 80302, USA.
Dr. **P. Czerski**	Associate Profesor of Histology and Head Department of Genetics National Research Institute of Mother and Child ul. Kasprzaka 17, 01-211 Warsaw, Poland
Dr. **B. Dieterich**	Director, Division of Environmental Health, World Health Organization Avenue Appia, 1211 Geneva 27, Switzerland
Dr. **J. D. Dumanskij**	Senior Research Worker, Institute of General and Communal Hygiene, Kirova 7, 252021-Kiev, USSR.

Dr. **Z. Edelwejn**
Associate Professor of Neurology,
Military Institute of Aviation Medicine,
ul. Krasińskiego 54,
01-755 Warsaw 86, Poland

Dr. **R. L. Elder**
Deputy Director,
Bureau of Radiological Health,
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852, USA.

Dr. **G. I. Evtušenko**
Director,
Institute of Industrial Hygiene and Occupational Diseases,
ul. Trinklera 6,
Harkov, USSR.

Dr. **M. Faber**
Professor and Director
The Finsen Laboratory,
The Finsen Institute,
Strandboulevarden 49
2100 Copenhagen, Denmark.

Mr. **Z. Frank**
Scientist,
Institute of Aviation Medicine,
Kovpakova 1,
16060 Prague 6, Czechoslovakia.

Dr. **J. C. Gallagher**
Professor, Bradford University,
Langarth
Woodland Grove, Weybridge Surrey KT 13 9 EQ,
United Kingdom.

Dr. **L. Goldstein**
Associate Professor of Psychiatry,
Institute for Mental Health Sciences,
Rutgers Medical School,
P. O. Box 101
Piscataway, New Jersey 08854, USA.

Dr. **Zinaida V. Gordon**
Professor and Head, Laboratory of Electromagnetic Fields,
Institute of Industrial Hygiene and Occupational Diseases
of the USSR Academy of Medical Sciences,
Meierovski Proezd 31,
Moscow, USSR.

Dr. **E. H. Grant**
Reader in Physics,
Physics Department,
Queen Elizabeth College
University of London
Campden Hill Road,
London W 8 7AH, UK.

Dr. **A. W. Guy**
Associate Professor,
Department of Rehabilitation Medicine,
School of Medicine,
University of Washington
Seattle, Washington 98195, USA.

Dr. **K. H. Illinger**	Associate Professor of Chemistry, Department of Chemistry, Tufts University, Medford, Massachussets 02155, USA.
Dr. **D. R. Justesen**	Director, Laboratories of Experimental Neuropsychology US Veterans Administration Hospital 4801 Linwood Boulevard Kansas City, Missouri 64128, USA.
Dr. **Taisia V. Kalada**	Head, Laboratory of Physical Agents Institute of Industrial Hygiene and Occupational Diseases, 2-aja Sovietskaja 4, Leningrad, USSR.
Dr. **Eliška Klimková-Deutschová**	Professor of Neurology, University Clinic Belohradska 130, 12000 Prague 2 Vinohrady, Czechoslovakia
Dr. **F. Kossel**	Professor and Director, Division of Radiation Hygiene, Ministry of Health, Ingolstädter Landstrasse 1, 8042 Neuherberg, Federal Republic of Germany.
Dr. **H. Kucia-Korniewicz**	Senior Research Worker, Central Institute of Labour Protection, Pl. Konstytucji 2, 00-552 Warsaw, Poland
Dr. **J. Kupfer**	Research Worker, German Central Institute for Occupational Medicine, Möldnerstrasse 40-42, 1034 Berlin German Democratic Republic.
Dr. **Evgenia A. Lobanova**	Senior Research Worker, Institute of Industrial Hygiene and Occupational Diseases of the USSR Academy of Medical Sciences Meierovski Proezd 31, Moscow, USSR
Dr. **S. Martner**	Industrial Physician, Telefonaktiebolaget L. M. Ericsson Hälso Sjukvården, 43120 Mölndal, Sweden
Dr. **S. M. Michaelson**	Professor Department Radiation Biology and Biophysics, School of Medicine and Dentistry, University of Rochester, Rochester, Nev York 14642, USA.

Dr. **W. A. Mills**
Director,
Criteria and Standards Division,
Office of Radiation Programs,
Environmental Protection Agency
5600 Fishers Lane,
Rockville, Maryland 20852, USA.

Dr. **H. Mikołajczyk**
Associate Professor of Endocrinology and Head,
Department of Physical Hazards,
Institute of Industrial Medicine
ul. Teresy 8,
91-348 Łódź, Poland.

Dr. **L. Miro**
Associate Professor of Biophysics,
Laboratory of Cellular Biology,
Faculty of Medicine,
Avenue Kennedy,
30 Nimes, France

Dr. **Kamila V. Nikonova**
Senior Research Worker,
Institute of Industrial Hygiene and Occupational Diseases of the USSR Academy of Medical Sciences.
Meierovski Proezd 31,
Moscow, USSR.

Dr. **K. Ostrowski**
Professor and Director,
Institute of Biostructure
Warsaw Medical Academy,
ul. Chałubińskiego 5,
02-004 Warsaw, Poland.

Dr. **Jana Pazderova**
Research Worker,
Clinic for Occupational Diseases,
Vysehradska 49,
Prague 2, Czechoslovakia.

Dr. **M. Piotrowski**
Senior Research Worker,
Military Institute of Hygiene and Epidemiology,
ul. Kozielska 4,
01-163 Warsaw, Poland

Dr. **C. Romero-Sierra**
Research Biologist,
Department of Anatomy,
Queen's University,
Kingston, Ontario, Canada.

Dr. **A. V. Roščin**
Professor and Director
Institute of Industrial Hygiene and Occupational Diseases of the USSR Academy of Medical Sciences,
Meierovski Proezd 31,
Moscow, USSR.

Dr. **R. Rugh**
Research Biologist,
Bureau of Radiological Health,
Food and Drug Administration,
5600 Fishers Lane
Rockville, Maryland 20852, USA.

Dr. **Maria N. Sadčikova**
Senior Research Worker,
Institute of Industrial Hygiene and Occupational Diseases of the USSR Academy of Medical Sciences,
Meierovski Proezd 31,
Moscow, USSR.

Dr. **H. P. Schwan**
Professor and Chairman,
Department of Biomedical Engineering
Moore School of Electrical Engineering,
University of Pensylvania,
200 South, 33nd Street
Philadelphia, Pensylvania 19104, USA.

Dr. **B. Servantie**
Research Worker,
Section of Cellular Biology,
Naval Centre for Applied Biophysical Studies and Research,
Sainte-Anne,
83-Toulon-Naval, France

Dr. **E. Shalmon**
Scientist,
Radiation Health, Unit World Health Organization
Avenue Appia,
1211 Geneva 27, Switzerland

Dr. **M. L. Shore**
Director,
Division of Biological Effects,
Bureau of Radiological Health,
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852, USA.

Dr. **M. Siekierzyński**
Specialist Internal Diseases,
Institute for Postgraduate Study,
Military Medical Academy,
ul. Szaserów 28,
04-306 Warsaw 60, Poland.

Dr. **Charlotte Silverman**
Deputy Director,
Division of Biological Effects,
Bureau of Radiological Health,
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852, USA.

Dr. **D. B. Smith**
Professor
Postgraduate School of Studies in Electrical and Electronic Engineering,
University of Bradford,
Bradford, Yorkshire BD 7 1-DP,
United Kingdom

Dr. **Wanda-Stodolnik-Barańska**
Head, Laboratory of Electron Microscopy,
Institute of Biostructure,
Warsaw Medical Academy,
ul. Chałubińskiego 5,
02-004 Warsaw, Poland.

Dr. **J. Štverak**	Research Worker, Institute of Aviation Medicine, Kovpakova 1, 16060 Prague 6, Czechoslovakia.
Dr. **M. J. Suess**	Regional Officer for Environmental Health, World Health Organization Regional Office for Europe 8, Scherfigsvej, 2100 Copenhagen, Denmark.
Dr. **C. Susskind**	Professor, Department of Electrical Engineering University of California Berkeley, California 94720, USA.
Dr. **B. M. Tengroth**	Professor and Head, Department of Ophthalmology, University of Göteborg Sahlgrenska sjukhuset 41345 Göteborg, Sweden.
Mr. **J. C. Villforth**	Director, Bureau of Radiological Health, Food and Drug Administration 5600 Fishers Lane Rockville, Maryland 20852, USA.
Dr. **W. A. G. Voss**	Professor, Department of Electrical Engineering The University of Alberta Edmonton, Alberta, Canada.
Dr. **B. Waldeskog**	Medical Physicist, Radiation Health Unit, World Health Organization Avenue Appia, 1211 Geneva 27, Switzerland.
Dr. **K. Yagi**	Research Worker, Tokyo Medical College Hospital 6—7 — I Nishishinjuku Shinjuku — ku, Japan.
Dr. **M. M. Zaret**	Director of Research, The Zaret Fundation Inc. 1230 Post Road Scarsdale, New York, 10583, USA.
Dr. **S. Żydecki**	Ophthalmologist Institute for Postgraduate Study, Military Medical Academy, ul. Szaserów 28, 04-306 Warsaw 60, Poland.

REPRESENTATIVES OF INTERNATIONAL ORGANIZATIONS

Commission of the European Communities
Mr. *A. Jolivet*
International Association of Radiation Protection Associations
  Dr. *M. Faber*
International Commission on Radiological Protection
  Dr. *M. Faber*
International Commission on Radiation Units and Measurements
  Dr. *A. Fränz*
International Society of Radiology
  Dr. *M. Siekierzyński*

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